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DEAN LEWIS

A BIOGRAPHIC SKETCH

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CHICAGO

Appraisal and appreciation of real achievement in a man's life comes too often as an epitaph. It is pleasant, therefore, to make one of the noteworthy exceptions in this Dean Lewis birthday issue of the ARCHIVES OF SURGERY, which, by their contributions to it, affords a few of his associates and pupils an opportunity of indicating for his many friends their admiration of his achievements and their affection for him as a man and of wishing him many more years of active and happy life.

To attempt to paint the picture of Dean Lewis (for those who know him) is a footless effort. Individualism and friendly aggressiveness often stand out as impressions on meeting him for the first time. As a student in his class in surgical anatomy I was struck by his complete dominance of the scene, his accurate and historical knowledge of his subject and his alertness to the reactions of his class and subconsciously by the fact that anatomy in his exposition of it was no longer a dead but a bright, living subject. This is an indirect way of saying that nearly all men are instantly attracted to him and that his great influence on the development of his pupils and associates is a natural result of obvious forces.

After his graduation in 1895 from Lake Forest College and in 1899 from Rush Medical College, where he came under the influence of Billings, Herrick, Senn and Bevan, he interned at Cook County Hospital, an institution which has made a deep and lasting impression on the surgical consciousness of the Middle West. With him as intern colleagues in the hospital were Rowan, Wells, Kanavel, Besley and Richter, and dominating the scene as attending surgeons were Fenger, Murphy, Ochsner, Andrews and Harris. A recital of these names, so well known to American surgeons, indicates that inspiration for hard work and good fellowship abounded.

On completion of his internship he accepted a position as instructor of anatomy at the University of Chicago and for four years arduously devoted himself to his task, with a consequent sound knowledge of

anatomy which, coupled with an unusual memory for its details, has often subsequently brought amazement to his colleagues and consternation to his medical students. Coming under the influence of Bensley, then professor of anatomy, he became interested in vital staining of tissue and, utilizing this technic, he reported the histologic changes and hyperplasia of the chromophile cells in the anterior lobe of the hypophysis in a case of acromegaly. In this period were included six months of graduate study with Spalteholz in Leipzig, Germany, where (by reconstruction models) the fascia of the kidney was the subject of study.

From 1903 to 1924, with the exception of the war years, Dean Lewis taught surgery at Rush Medical College and carried on an increasing surgical practice at the Presbyterian Hospital. He became professor of surgery in 1920 and shared with Bevan the burden of teaching and direction of surgical activities.

It was in this stretch of years that he became exposed and succumbed to the wiles and attractions of travel. His reputation as a teacher and then as a surgeon and a contributor to progressive surgical thought grew steadily, and he was in demand throughout the Middle West and the West as a consultant surgeon, an operating surgeon and a speaker. His leadership in diffusion of sound surgical and pathologic knowledge was everywhere acknowledged. His many contributions concerned themselves with ductless glands, transplantation of tissue, bone tumors, neurosurgery and pathologic studies of the breast which were the results of both clinical and experimental studies. A noteworthy happening during this period was the first clinical use of ethylene as an anesthetic by Dr. Lewis at the Presbyterian Hospital. Subsequently, "Clinical Experiences with Ethylene Oxygen Anaesthesia" was published by A. B. Luckhardt, the discoverer of ethylene, and Dean Lewis, in December 1923.

As a teacher he provokes the greatest interest on the part of his students and colleagues, not only because he commands their respect for his clinical knowledge of the subject and the relation of the fundamental sciences and of medical history to it but because he conducts his clinic in the manner of a dialogue, which in the course of events demands answers to questions. This requires an agility of mind and a breadth of knowledge that few of his students and associates easily command, and, as a consequence, succeeding classes carry away, in addition to the clinical instruction, knowledge of many anatomic, pathologic and historical facts. The mere mention to his former students of the claw-hand and the lumbricales, "Madame" Dejerine, Rokitansky, Nicoladoni or Astley Cooper will recall a few of the inquiries posed by an inspiring teacher.

The World War played an important role in Dean Lewis' life and in some ways may have been one of its happiest periods. Having a deep

regard for his country and for the soldiers of the line who were serving it, enjoying the society of his fellow men, resourceful in unexpected situations and having real ability as an organizer and sufficient physical stamina to carry on, he made his service a notable one. Let the record speak for itself. He was commissioned a major in the medical corps of the United States Army in the spring of 1917 and was directed to organize Base Hospital No. 13 at the Presbyterian Hospital, Chicago. In December 1917 he was ordered to active duty with his organization at Fort McPherson, Ga., and shortly afterward was sent to the University of Michigan to conduct research on regeneration of nerves with Dr. G. Carl Huber. This work resulted in valuable information on the method of formation and prevention of neuromas. About May 1, 1918 he rejoined Base Hospital No. 13 at Camp Merritt, N. J. He sailed for France on May 18, arriving in June in Limoges, where Base Hospital No. 13 was permanently established. On July 8, he was sent to the American headquarters at Chaumont as the head of a surgical team consisting of three officers, two nurses and two orderlies and was assigned to work at Evacuation Hospital No. 7 at Coulommiers. After two weeks of very active service there he was transferred to Evacuation Hospital No. 6 at Chateau-Thierry, and on August 19 he was given command of the surgical service at Evacuation Hospital No. 5, which was also located at Chateau-Thierry. He continued to work with this hospital until the end of the war. During this period it was stationed at Juvigny from August 29 to September 14, taking care of the wounded from the Thirty-Second Division during the Verdun offensive. It was then moved to Villers-Cotterets, where it was set up in readiness to evacuate the wounded from the St. Mihiel sector. About September 29 the hospital was moved to LaVeuve, where it functioned until October 16, taking care of the wounded from the Second Division and from the Thirty-Sixth Division during the Champagne offensive. In the final days of the war his hospital was stationed at Staden, Belgium, working with the Thirty-Seventh Division and also with the Ninety-First. After the armistice Major Lewis was returned to Base Hospital No. 13 and was promoted to the rank of lieutenant-colonel of the United States Army. On December 28 he returned to the United States and was placed in command of United States General Hospital No. 28 at Fort Sheridan, Ill., where a large portion of the service consisted of treatment of nerve injuries and reconstructive surgical procedures. In August 1919 he was honorably discharged from the service, and some months later the United States government, in recognition of his services, accorded him the distinguished service medal.

After his discharge from the army he returned to his teaching and practice at Rush Medical College and the Presbyterian Hospital. In 1920 he accepted the editorship of the ARCHIVES OF SURGERY, which he

has continued to devote his energies to making one of the significant surgical journals of the day. He received offers from several medical schools to head their departments of surgery, but it was not until January 1925 that he accepted the professorship of surgery at the University of Illinois Medical School. This position he occupied for only six months, as he then accepted the professorship of surgery at Johns Hopkins University, where he succeeded Dr. William S. Halsted.

Dr. Lewis' work and accomplishments at Johns Hopkins are well known. He found himself among friends of many years' standing, who made him welcome and have ably supported his leadership in teaching, investigation and the training of young men. During this period Dr. Lewis has been particularly interested in and has contributed largely to the knowledge of the relation of sex hormones to tumor growth. He has edited the widely used "Practice of Surgery," published by Prior, and it is in these volumes that his own classic work on peripheral nerve injuries and regeneration of nerves appears.

I should like to quote a paragraph from a letter written to me by one of his Baltimore and Johns Hopkins Hospital colleagues. Speaking of Dean Lewis, he said, "His Friday clinics to the third and fourth year medical students were among the best and most scholarly presentations of surgical discussions that I have ever listened to. In these and in other teaching exercises he displayed a remarkable familiarity with the surgical literature of the whole modern world and a memory that was astonishing in its accuracy. He was particularly interested in the surgery of peripheral nerves, tendons, joints and bones, and in these fields, which many general surgeons rather neglect, he showed a mastery of the subject and an operative facility which was remarkable. During his entire time here he laid great emphasis on the relationship of anatomy to surgery and also on acquaintance with the unusual types of infections such as actinomycosis, sporotrichosis, etc. He turned out from the residency of the surgical service at the Johns Hopkins Hospital a number of extremely able young men, many of whom have secured positions of importance as teachers and staff members of universities and hospitals."

Emerson has justly said that too many times one is weighed down by facts and forgets principles. This imperfect record of Dean Lewis has perhaps had in it too much of facts and too little of the man. What stands out, then, above the facts? A host of friends who know the greatness of his soul, his loyalty, his matchless spirit, his love of sports, his great ability as a surgeon and his comradeship salute him and wish him long life and well deserved happiness.

CHONDRODYSPLASIA

REPORT OF A CASE

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A patient came under my care in December 1939 with acute appendicitis. He presented such a multitude of skeletal tumors that after his recovery from the operation for appendicitis a study was made, and the case was deemed worthy of report. This was not so much because of the rarity of the lesion as because of the number and extent of the tumors, 91 being revealed on the roentgenograms. The condition conformed to the pattern of hereditary deforming chondrodysplasia in that numerous tumors were present, accompanied with skeletal deformities which arose between childhood and maturity and involved bones developed from cartilage. The component parts of each bony system, with the exception of those developed from membrane, showed such involvement.

In addition to the outward projections from the cortical regions giving rise to deformities, inward projections with the formation of central lesions were present. According to Geschickter and Copeland, "the fundamental basis of the congenital disturbance is obscure, but deficiencies in the periosteum and a tendency for the perichondrium to persist and to function as such, together with precartilaginous connective tissue about the joints, seem to be responsible for most of the deformities."

REPORT OF CASE

The patient, a man aged 25, was one of ten children. He stated that three of his brothers (not available for examination) had similar tumor masses and deformities, none as numerous or as large as his own. The remaining brother and his five sisters showed no visible evidence of the disease. There was a history of similar tumors in the father, but none had occurred in the mother or in the older generations of the family so far as he knew. His first bony deformity was noted by his parents when he was 1 year old. At the age of 11 years he was admitted to the Children's Hospital. The records show that in June 1925 bony tumors were removed from the left outer malleolus and from the lower end of the left ulna, microscopic examination of which confirmed the clinical diagnosis of benign osteochondroma. Roentgen examination at that time showed "multiple exostoses of nearly all the long bones." Throughout childhood and adolescence numerous tumors appeared, some of which grew steadily, producing deformities about the larger joints of the extremities. During the last four years, since reaching maturity, he had noted no further increase in size of any of the tumor masses and no change in any of the deformities of the extremities. He gave no history of

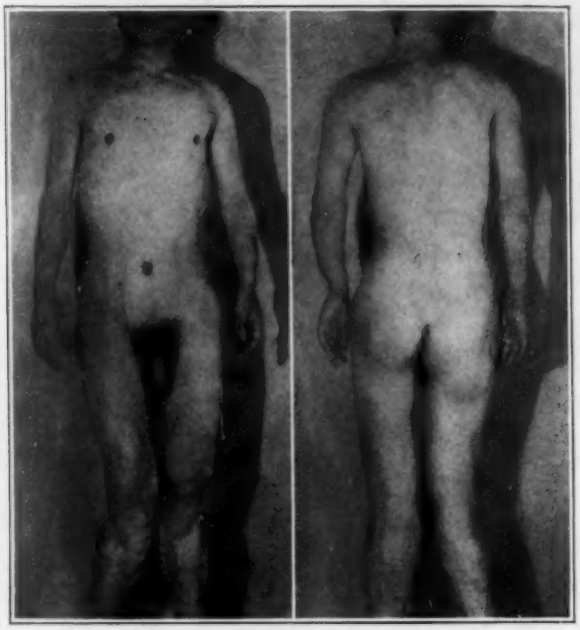

Fig. 1.—Photographs of the patient.

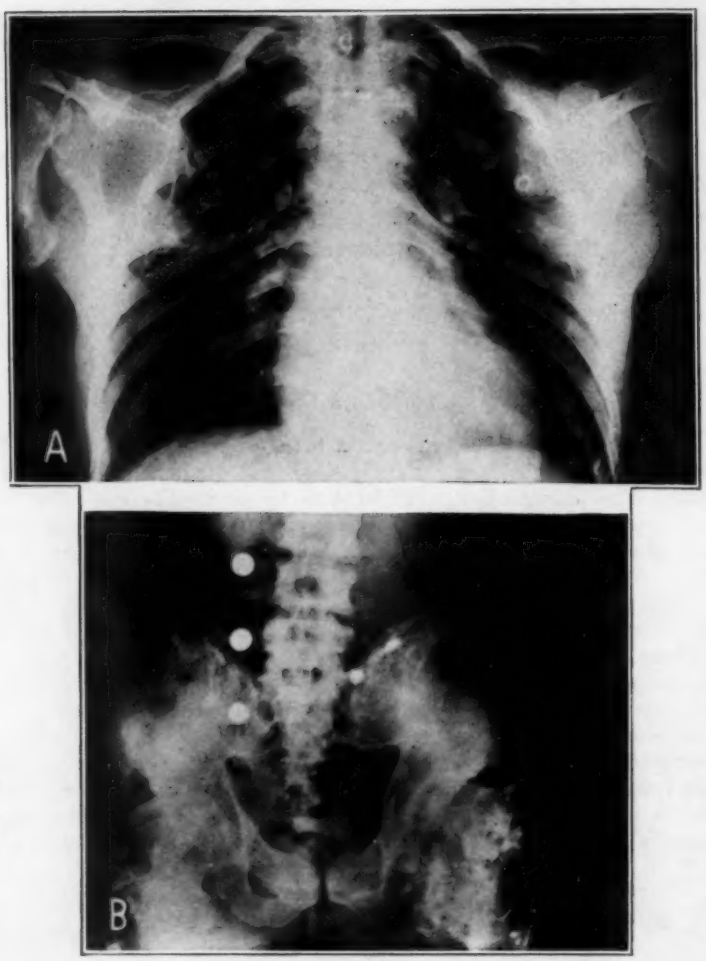

Fig. 2.—*A*, ribs and sternum; *B*, pelvis and hip joints.

pain associated with the tumors and complained of no dysfunction other than a limp due to shortening of the right leg and a limitation of motion in the left wrist.

Physical examination revealed the heart, lungs, blood pressure, blood and urine to be normal.

His height was 5 feet and 10 inches (177.8 cm.). His weight was 132 pounds (59.9 Kg.).

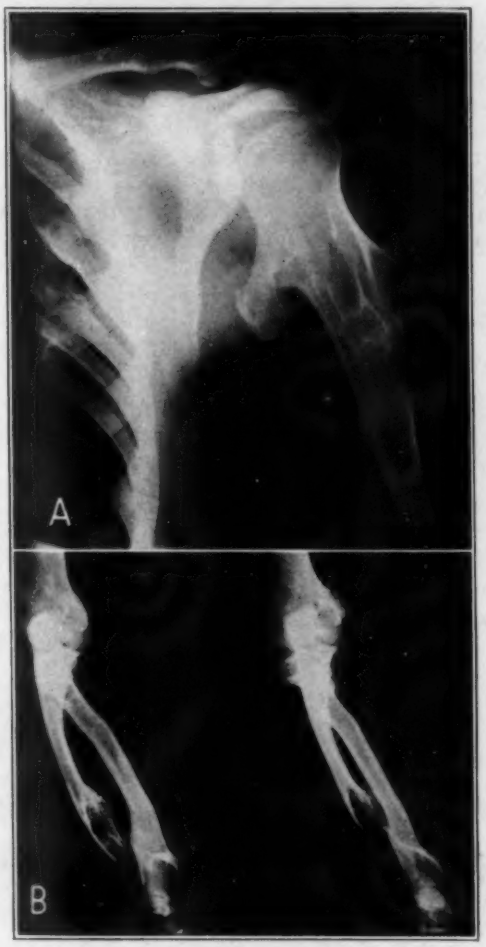

Fig. 3.—*A*, left shoulder and upper part of humerus; *B*, left elbow, radius and ulna.

The head and neck were apparently normal, with no visible or palpable bony deformities.

The patient stood with the pelvis tilted to the right and presented a moderate structural "right lumbar, left dorsal" scoliosis. There was some rotation of the

vertebrae, causing prominence of the right paravertebral region, especially noticeable in flexion. Motions of the back were free, with complete range of flexion and extension but slight restriction of lateral bending and rotation. There were small palpable irregularities and tumor masses on the medial border and posterior surface of the right scapula. The spine of the left scapula presented small palpable tumor masses, and its posterior surface also was nodular and irregular. There were numerous small conical masses arising from the ribs, but there was no marked deformity of the thorax as a whole. Palpable nodules were present over the pelvis.

All four extremities presented varying-sized, bony, hard tumor masses attached to the ends of the long bones. These tumors were of different shapes, some smooth and rounded, some nodular and some sharp. In several areas there were compound masses with multiple projecting processes. The tumors were not tender and were not attached to the skin or to the soft tissues. In addition to the tumor masses there were numerous deformities, the left upper and the right lower extremities being most severely involved. The lengths of similar portions of the extremities were different on the two sides, comparable measurements being as follows:

	Right	Left
Upper		
Acromion to olecranon	12 inches (30.4 cm.)	11 inches (27.9 cm.)
External condyle to radial styloid process	9½ inches (24 cm.)	8½ inches (21.5 cm.)
External condyle to ulnar styloid process	9 inches (22.8 cm.)	6½ inches (16.4 cm.)
Lower		
Anterior superior iliac spine to internal malleolus	34½ inches (87.5 cm.)	35⅞ inches (91 cm.)
Anterior superior iliac spine to patella	16½ inches (41.8 cm.)	17¾ inches (45 cm.)

Left Upper Extremity.—There was a rounded, smooth bony tumor 1 inch (2.5 cm.) in diameter attached to the medial aspect of the humerus, presenting in the axilla. There was no restriction of motion of the shoulder. The shaft of the humerus was smooth and straight. In the region of the elbow there was a small, irregular tumor mass apparently arising from the medial epicondyle. The head of the radius was prominent and palpably enlarged from tumorous overgrowth. The axis of the elbow joint and the carrying angle were approximately normal. Flexion and extension of the elbow were approximately normal. There were operative scars over the lower end of the radius and ulna, with rounded masses attached to the radius. The ulna was markedly shortened, throwing the wrist into about 40 degrees of adduction. Flexion and extension of the wrist were limited about 10 per cent, and there was over 50 per cent limitation of supination. There were several small pointed tumor masses arising from the metacarpal bones and the phalanges near the joints, causing slight deformity and limitation of motion. The fourth metacarpal bone was approximately ½ inch (1.2 cm.) shorter than normal, the head being depressed and palpable in the palm.

Right Upper Extremity.—There were a few palpable tumor masses arising from the upper end of the humerus, but there was no deformity and no limitation of motion of the shoulder. There were a 1 inch (2.5 cm.) rounded tumor mass in the region of the medial epicondyle and 5 degrees of cubitus varus deformity of the elbow. Flexion and extension of the elbow were complete, but there was very slight limitation of pronation and supination. There was a small pointed tumor

arising from the distal third of the ulna, but there was no deviation from the normal relation between the radial and the ulnar styloid processes. There was no apparent involvement of the carpal or the metacarpal bones, but there were small tumor masses on the phalanges of all five fingers. There was very slight angulation deformity of the second, fourth and fifth fingers but no restriction of motion.

Fig. 4.—*A*, right shoulder and upper part of humerus; *B*, right elbow, radius and ulna.

Left Lower Extremity.—There was no apparent deformity around the left hip. There were diffuse grating on motion of the hip and limitation of abduction to about 30 degrees. There was no limitation of flexion, extension or rotation. The greater trochanter was in its normal relation, but there was palpable irregular enlargement of the upper end of the shaft and the neck of the femur. The thigh

was apparently normal, but in the region of the knee there were fairly large rounded nodules palpable on the medial and lateral aspects of the lower end of the femur. There was complete range of motion at the knee. There was a large compound tumor mass about 3 inches (7.6 cm.) in diameter on the medial aspect of the upper end of the tibia, causing about 10 degrees valgus offset of the shaft on the diaphysis. There likewise were small rounded protuberances over the upper

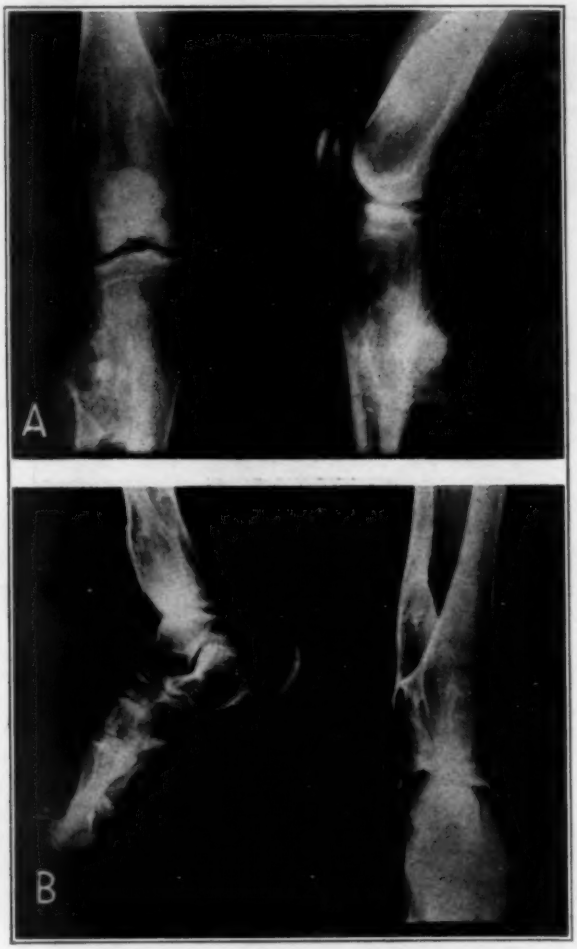

Fig. 5.—*A*, left knee; *B*, left ankle and foot.

end of the fibula. There were numerous rounded and pointed masses around the lower ends of both the tibia and the fibula, but there was free motion of the ankle joint. However, marked talipes valgus was present. The foot was broad and short, and a few irregularities were palpable in the metatarsal bones. The great toe was apparently normal. There was a severe congenital anomaly involving the other

toes. The third and fourth were displaced dorsally above the second and fifth, and there was a partially developed supernumerary digit between the third and the fourth.

Right Lower Extremity.—There was no restriction of motion of the hip, but there was a compound tumor mass about 4 inches (10 cm.) long and 3 inches (8.6 cm.) wide, palpable posterior to and below the greater trochanter. The thigh

Fig. 6.—*A*, right knee; *B*, right ankle and foot.

was normal, but there was a severe deformity of the right knee, due to tumor masses arising from the lower end of the femur and the upper end of the tibia. The knee lacked 15 degrees of complete extension. There were 20 degrees of valgus deformity and about 15 degrees of external rotation at the knee. There were large compound tumor masses arising from the medial side of the femur and tibia,

causing discoloration of the skin over their prominences. There also was marked enlargement and dilatation of the saphenous vein. There were small tumor masses on the lateral aspects of the lower part of the fibula and the upper part of the tibia. In the region of the ankle there were scars from previous operative removal of tumor masses, but there were numerous small nodular masses still present around both malleoli. There was slight talipes valgus of the foot but no other deformity, and few small tumor masses were palpable.

SUMMARY

A case of chondrodysplasia in a man aged 25 is presented.

THE PLACE OF THE GASTROSCOPE IN THE DIAGNOSIS OF LESIONS OF THE STOMACH AND OF THE DUODENUM

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The great contributions which have been responsible for the present knowledge of lesions of the stomach and of the duodenum have been the facts disclosed by surgical treatment of these lesions during the life of the patient, the development of roentgenology, which shows by indirect means the site and character of these lesions, and the development of the flexible gastroscope. The development of endoscopy has been a spectacular feature of modern diagnostic methods, and those instruments which have for their purpose the visualization of cavities of the body are some of the most ingenious and useful examples of the instrument maker's art. It was inevitable in all this development that some satisfactory means should be devised for visualizing the interior of the stomach. For many years physicians had to be content with an inadequate, rigid instrument, but the flexible gastroscope has opened a new field and has proved that it is possible to obtain a satisfactory view of the interior of the stomach in almost all cases. It is difficult to visualize two portions of the stomach: a narrow strip of the posterior wall, along which the gastroscope rests and which cannot be separated far enough from the lens of the gastroscope for adequate visualization, and a small segment of the lesser curvature of the antral portion, just beyond the angle. There are a few cases in which the difficulties in using the instrument are such that this type of examination is contraindicated, but these cases form only a very small per cent of the cases in which gastroscopic examination is advisable. Enough experience has now been obtained in the use of this instrument to give some idea of its value and its contributions to knowledge of lesions of the stomach and of the duodenum.

When it was learned that the gastroscope would give a satisfactory view of the interior of the stomach, one of the first questions which the members of the medical profession sought to answer was in relation to gastritis. It was generally accepted that gastritis is the most frequent of all pathologic conditions of the stomach, but there was vagueness as to how gastritis should be classified from the standpoint of symptomatology

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and the relation of the symptoms to the various stages. Similarly, a satisfactory answer had not been given regarding the relation of gastritis to organic lesions of the stomach, particularly to ulcer and carcinoma. The claim made by many observers that gastritis is a precursor of ulcer and is the chief factor in disappointing results following operation for ulcer has been difficult to evaluate. The basis for this claim is somewhat theoretic, but certain clinical and experimental evidence supports it. For example, it has been shown that the use of cinchophen in animals produces a sequence of events culminating in chronic ulcer, in which gastritis in various stages associated with multiple ulcerations precedes the formation of the chronic lesion.[1] Any method which would permit one to identify these different stages of gastritis clinically, to observe the circumstances under which they develop, to correlate the symptoms with the pathologic picture and to determine whether these changes are liable to be followed by chronic ulcer would be a great contribution toward a more intelligent understanding of both benign and malignant lesions of the stomach. It is in this respect that the flexible gastroscope offers so much. As yet there is much to be determined, but a vast amount of information is rapidly accumulating which may be applied to a better understanding of these questions.

In cases of duodenal ulcer the gastroscope has not as yet been of much value, since it is impossible to visualize the duodenum, and only those changes which are secondary to an ulcer can be identified. But in this respect the gastroscopic examination may be valuable, for the decision as to treatment may be determined by the finding of a deformity secondary to ulcer. Similarly, gastroscopic examination may disclose important data in respect to results of operation for duodenal ulcer. This is true in cases in which disappointing results follow surgical management of ulcer, regardless of the operation which has been carried out, and particularly in those cases in which operation involves the use of the jejunum either in gastroenterostomy or after partial gastrectomy. One of the puzzling problems in connection with surgical treatment of duodenal ulcer has been that of interpretation of some of the symptoms which may occasionally recur after operation. In this respect the gastroscope is proving to be a welcome aid in obtaining accurate information, for the skilled gastroscopist is enabled not only to study the operative stoma, which may be under inspection, and report on its actual appearance but to study the adjacent portions of the loops of the intestine which were associated with it.

In cases of gastric ulcer the chief value of the gastroscope is in the differential diagnosis of benign and malignant ulcer. Enough evidence

1. Stalker, L. K.: Experimental Cinchophen Peptic Ulcers, Thesis, University of Minnesota Graduate School, 1937.

has now accumulated to show that by this method such lesions can be studied so directly as to give valuable information in determining whether or not the ulcer is malignant. I do not believe that the method has reached the point of absolute dependability, yet the knowledge which has been acquired in the relatively short time in which the instrument has been used seems to indicate that, more than any other method except microscopic examination, it will probably contribute to the surgeon's ability to differentiate these lesions. Similarly, the method makes it possible to locate other, smaller lesions which may have been overlooked in a case of gastric cancer. It is also true, although of rare occurrence, that roentgen examination may fail to detect a small cancer in the fundus of the stomach, yet the lesion may be readily identified by a competent gastroscopist. The gastroscope also permits identification of the type of cancer and enables one to determine whether multiple lesions are present. Of the greatest importance is the fact that it may give information as to the operability of the growth.

It is in the study of the stomach after operation that the flexible gastroscope has such interesting possibilities. Until this instrument was developed to a point at which a satisfactory inspection of the stomach could be made, the interpretation of symptoms persisting after operations for benign lesions of the stomach was, to some extent, conjecture. It is probably for this reason that there was such a great discrepancy in the figures reported from various clinics as to the results of various types of operations, since the relation between symptoms and pathologic change in the stomach after operation is on a much less definite basis than when no operation has been carried out. While roentgenology contributed much knowledge in this particular group of cases, the roentgenologist was the first to recognize the fact that there were definite limitations in the story the roentgenoscope and the roentgenogram could tell of the postoperative condition of the stomach, particularly in those cases in which extensive reconstruction operations had been part of the surgical procedure. The increasing accuracy of the flexible gastroscope in enabling one to view practically all parts of the stomach has been a boon to both the clinician and the surgeon in evaluating symptoms following operation and also in providing evidence as to the effectiveness of various types of operation. Some surprising points have already been brought out by Schindler and his associates [2] and by Moersch and Walters [3] in gastroscopic studies after operation.

2. Schindler, R., and Gold, R. L.: Gastroscopy in Gastric Carcinoma Especially in Its Early Diagnosis, Surg., Gynec. & Obst. **69**:1-17 (July) 1939. Schindler, R.; Necheles, H., and Gold, R. L.: Surgical Gastritis: A Study of the Genesis Found in Resected Stomachs with Particular Reference to the So-Called "Antral Gastritis" Associated with Ulcer, ibid. **69**:281-286 (Sept.) 1939.

3. Moersch, H. J., and Walters, W.: Unpublished data.

The latter observers recently studied a series of more than 100 cases in which various types of operations were carried out. Some interesting observations were made possible by this study, particularly in relation to the incidence of gastritis, which has been such a controversial point in regard to the relation of gastritis to persisting symptoms after operation. For example, in about a third of the cases in which gastroenterostomy was done for duodenal ulcer and in which sufficient symptoms persisted to require a subsequent thorough examination, gastroscopic study revealed that the stomach was apparently entirely normal. Although Schindler, in his report of postoperative gastroscopic examinations, noted a much smaller percentage of normal stomachs after operation, Moersch and Walters pointed out that this disagreement is probably due to difference in opinion as to what constitutes normal gastric mucosa and early changes of gastritis. They also pointed out that the gastroscopic picture may change markedly after an acute infectious process or an indiscretion in diet. The feeling that "the longer the period which is allowed to elapse between a surgical procedure on the stomach and gastroscopic examination, the less likely is gastritis to occur" was not found true in this series. The question of what accounts for gastric distress in those cases in which the stomach is normal as far as the gastroscope is concerned introduces the fact that functional disturbances are apparently frequently the predominant elements in the symptoms both before and after operation. Approximately two thirds of the patients who were subjected to gastroenterostomy for duodenal ulcer and in whom completely satisfactory results did not follow the operation showed evidence of gastritis, and almost every variety of gastritis might be seen in the same stomach. Moersch and Walters pointed out that one variety, which they classified as erosive gastritis, seemed not only to produce distinct symptoms but to respond satisfactorily to therapeutic management. This type of gastritis is characterized by multiple small erosions. In a small group of cases in which gastroenterostomy was done for duodenal ulcer there was a history of gastric bleeding at some time after the gastroenterostomy, and the clinical history was suggestive of gastrojejunal ulcer. In the cases in which another operation was performed the lesion which was found was erosive gastritis associated with gastrojejunitis rather than a typical gastrojejunal ulcer. The appearance of the stomach after partial gastrectomy is particularly interesting because of the still debated question as to the permanent effectiveness of partial gastrectomy in dealing with duodenal ulcer. In a third of these cases no abnormality was detected in the gastric or the jejunal mucosa, and in this group, as in cases in which gastroenterostomy was performed, satisfactory control of the symptoms was obtained by medical measures. There was a high incidence of erosive gastritis,

but fortunately this also seemed to respond satisfactorily to adequate medical management. In a group of cases of gastric ulcer in which an opportunity was given for subsequent gastroscopic examination, the majority of the patients had been subjected to excision of the ulcer and gastroenterostomy, and a smaller number had undergone a partial gastrectomy. There apparently was approximately the same relation of gastritis in this group of cases as was found in the preceding groups, with the additional finding of carcinoma in a sufficient percentage of cases to illustrate the close relation of gastric ulcer and gastric carcinoma.

In a general way, the study which Moersch and Walters have recently completed has given important information as to the appearance of the stomach after various types of operations for various lesions. The important feature of the study is that the high incidence of gastritis is a probable factor in the persistence of symptoms. Further studies of the stomach after operation will probably, if carried out on a sufficient number of patients who have not had recurrence of symptoms after operation, furnish further important information on this interesting point. Therefore, it may be anticipated that it will be possible to evaluate much more accurately the cause of symptoms following operation for peptic ulcer and to deal more intelligently with them.

Permission was granted by Drs. Moersch and Walters to use statistics prepared in connection with their postoperative study of the stomach, which has not yet been published.

BORDERLINE PROBLEMS IN THE DIGESTIVE FIELD

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Notwithstanding the increasing penetration of surgery into many other fields, cardiovascular, respiratory, renal, neural and endocrine, I feel sure that the digestive tract presents by far the most borderline problems, in which one must decide in each individual case whether surgical or nonsurgical treatment is the more likely to bring about cure or improvement. To operate or not to operate for peptic ulcer, gastric or duodenal, disease of the gallbladder, chronic appendicitis, cancer of the esophagus, stomach or small and large intestine or nonspecific ulcerative colitis—that is the question; and, if operation is decided on, when to operate, what operation to perform and who is to operate. On the proper answers to these questions depend in large measure the end results in each case.

While the main purpose of this short paper is to discuss treatment, it is axiomatic that for the optimum results correct diagnosis or, at least, a diagnosis of maximum probability is essential. But diagnosis of many intra-abdominal conditions is often extremely difficult, and it is only by the closest cooperation of internist and surgeon as well as by utilization of all appropriate technical methods that error can be reduced to a minimum. One may like to agree with Neusser that "the history of the case should give us our correct diagnosis, the physical examination and laboratory findings should be merely confirmatory" or to believe with Hilton that "every pain has its distinct and pregnant significance if we will but carefully search for it," but in the abdominal field this is sometimes not enough. Nevertheless, it is obviously essential that in every case a careful and thoroughly digested history should be taken and an especially painstaking analysis should be made of the symptom *pain*—the symptom that usually brings the patient to the physician—for in many cases it is the best means of reaching a correct diagnosis or at least of obtaining a valuable clue.

But pain is often a fragile reed on which to lean, for there are few if any pain fibers in the viscera, and with a viscerosensory reflex as the best explanation of abdominal pain, with the similarity of the nerve supply to abdominal and thoracic organs, with the close proximity of the various abdominal organs to each other (for example, the gallbladder, the pylorus, the duodenum, the hepatic flexure or the appendix, the

right ovary and tube and the ureter) and the relatively thin diaphragm all that separates the lower thoracic from the upper abdominal organs, is it any wonder that the pain picture is often confusing, that symptoms often overlap, that referred pain is so common and that the true interpretation of a given pain is difficult and sometimes impossible?

It is worth remembering in this connection that Dean Lewis in his "Practice of Surgery" mentioned six other conditions which simulate the pain of disease of the gallbladder and no less than twenty-nine which simulate that of acute appendicitis, and in every case there are those unpredictable variables, the enormous variation in the individual response to stimuli and the large role the psyche plays in sensory interpretation. Thus, while each case should be studied with the most meticulous care by the internist as well as the surgeon, for each approaches the problem from a somewhat different angle and each may discover something which the other may have missed, and while each case must be regarded as presenting a special problem of research to be attacked by "that insatiable intellectual curiosity that differentiates man from the beast," there will probably always remain a small group in which one is obliged to agree with Charles Mayo that "sometimes our best means of diagnosis is the memory of what we found in the abdomen when an exploratory operation was performed months or perhaps years previously upon a patient presenting a similar clinical picture."

Many of the organic diseases of the digestive tract are obviously potentially "surgical" as regards treatment. But surgical treatment is a two-edged sword—it takes away but it also gives; it removes organic disease—ulcer, diseases of the gallbladder or appendicitis—at a surprisingly low mortality rate in the hands of a skilled surgeon, but with the best technic there is always the possibility of formation of adhesions bringing about greater or less obstruction or impairment of function, while certain operations in their very essence leave behind an abnormal physiologic picture—for example, gastroenterostomy, ileostomy, ileosigmoidostomy or cholecystogastrostomy. With care and time certain of these unphysiologic states may produce few or even no symptoms, but sometimes the state of the patient may be no better than before he was treated surgically. From a month's census of all new patients admitted to this clinic, one fourth of the total number had been previously operated on but had returned complaining of the same symptoms or of new symptoms.

On the other hand, the surgeon is prone to forget that functional disturbances do not disappear with the removal of their organic cause; it may take months or even years of careful postoperative treatment to conquer these functional habits—pylorospasm, hyperchlorhydria, or gastric or intestinal dyspepsia—and it is lack of realization of this that

has converted many potential cures into relative or complete failures. The surgeon is keenly aware of the immediate results of the operation, results due in some measure to the rest and proper care in the hospital incidental to the operation. He is far too often ignorant of the late results of supposedly successful operations, for, if old symptoms persist or new symptoms arise, the patient frequently does not return to the same surgeon but consults an internist or another surgeon.

I shall discuss briefly certain of these borderline conditions. It is axiomatic that the more definite the need for surgical attack, the greater the likelihood of a permanently successful result. Thus, the percentage of cures is much higher in cases of cholelithiasis with frequently recurring attacks of pain, in cases of gastric or duodenal ulcer with gross organic obstruction and in cases of acute or recurrent appendicitis than in cases of chronic cholecystitis without stone, nonobstructing peptic ulcer or chronic appendicitis. The greater the need, the more clearcut the picture, the better the end result!

PEPTIC ULCER, GASTRIC OR DUODENAL

The question of peptic ulcer was once the great battleground:

> "Each champion to the other's virtue blind
> And thinks his treatment only cures mankind";

but it is now the scene of few controversies, for the lion and the lamb lie down peacefully together, and the lamb is often more bloodthirsty than the lion. The borderline problems in this field, however, are still interesting.

How much do the obstructive symptoms depend on organic stricture, which is "surgical"; how much on inflammation, spasm and edema, which may be relieved by nonsurgical measures?

How many large hemorrhages should a patient have before being operated on? In most cases two or three, not more. Should the operation be performed at the time of the bleeding because the source of many hemorrhages is difficult to find in the interval between bleedings, being often a minute ulcer or erosion, often tucked between mucosal folds?

How often is potential malignancy a reason for operation? Never in the case of duodenal ulcer, but certainly always in the case of gastric ulcer if the lesion does not respond to treatment, if occult blood persists in the stool or if the roentgen defect is large and persistent under a regimen of rest, soft diet and time. And yet in my series only 5 per cent of gastric ulcers became malignant; in two relatively recent German series, only 1.8 per cent and 3 per cent respectively.

If there are perigastric or periduodenal adhesions which do not obstruct but which render normal physiologic function difficult, how long should one try dietetic and physical measures before advising operation?

Many patients can be kept surprisingly comfortable if they are willing or able to follow certain rules as regards diet and general hygiene, sometimes supplemented by simple medication, but with the American patient, at least, this is not easy; he chafes at restrictions; he demands quick results. Just as in the cure of acute ulcer, any one, with a very simple diet, can usually quickly relieve the symptoms. Very few have the personality and the persistence to persuade the patient of the necessity of a long course of after-treatment. Yet, if operation is finally decided on, this is the type least likely to respond satisfactorily.

If operation is decided on, what shall the operation be? Gastroenterostomy is brilliantly successful in cases of gross obstruction, but in my experience it is usually disappointing when there is no obstruction or only very slight obstruction. It drains the stomach and gives partial rest to the ulcer, but it does not stop hemorrhage, and it is essentially nonphysiologic. It is not without justification that the Germans speak of *"diese Krankheit-Gastroenterostomie"* or that Horder said, "the operation should be regarded as the first step in treatment and not the last."

Should one, in certain cases of gastric ulcer in which resection is extremely difficult, utilize jejunostomy more, so that one may see whether long rest and freedom from local irritation may bring about a cure? In my hands, the best results have been obtained by the smaller resections —pyloroplasty (possible only in a relatively small percentage of cases and performed well by the very few), gastroduodenostomy, the Polya operation, etc., but a great many able surgeons believe that in very large resections lies the only hope not only of curing ulcer but of preventing its recurrence and that it is only by removing the entire acid-stimulating portion of the stomach that this can be brought about. Are they right? Time only can tell.

The treatment of ulcer is a very complicated problem, and the key has not yet been found, for ulcer is not only a local problem, it is constitutional; it is a state of body and a state of mind as well. Every one knows the enormous role that emotional disturbances play in the recrudescence and possibly even in the origin of ulcer. It is known that centers of parasympathetic control lie in the hypothalamus, that stimulation of this area in animals causes increase of hydrochloric acid secretion and of gastric motility, that cardiospasm and megaesophagus arise experimentally if all branches of the vagus nerve to the stomach and the duodenum are cut but not if the pyloric branch to the vagus is spared and that with certain intracranial lesions, notably pituitary and hypothalamic, peptic ulceration may occur. Does this suggest that in certain cases vagotomy or vagectomy should supplant the more gross operation on the stomach and duodenum in the treatment of ulcer?

CHRONIC APPENDICITIS

Does such a condition exist? Some surgeons believe not, but I am sure they are wrong. Why should the appendix be denied the privilege of chronic disease? Every other organ enjoys it. But the diagnosis as usually made is undeniably wrong. In most cases it is but a part of a low grade inflammatory process involving the terminal part of the ileum, the cecum and the ascending colon, usually associated with visceroptosis, chronic constipation and an atonic, thin-walled cecum. Appendectomy is harmful and simply intensifies the patient's symptoms.

But I am equally sure that there is a very small group of cases of true chronic inflammation, often with no history of an acute attack, sometimes with a vague memory of an abdominal attack (usually undiagnosed) many years before. Gaither and I reported 47 such cases, in which the symptoms were rarely in the right lower quadrant of the abdomen, but usually were referred to the epigastric region and simulated a hyperacid, hypersthenic dyspeptic syndrome, a periodic syndrome characteristic of peptic ulcer or (very occasionally) of colitis. The fact that these symptoms, previously refractory to treatment, entirely disappeared after the appendectomy and that marked gross and microscopic pathologic changes were observed made us feel that the cases were true examples of chronic appendicitis.

We were much helped in our diagnosis by serial fluoroscopic studies, especially those extending over several days. There was visualized an appendix of abnormal size or, more often, of abnormal and often extremely bizarre form, and one in which the barium sulfate remained for a long time, in 1 case more than a week, after active purgation with magnesium sulfate.

CANCER

For cancer of the digestive tract nonsurgical treatment is purely—and poorly—palliative. In this field, at least, deep high voltage roentgen and radium therapy has been bitterly disappointing except in a few rare instances, usually of conditions of mesoblastic origin, while colloid selenium and colloid lead are equally ineffective. But to increase the percentage of cures (and cures have been none too frequent up to the present) it is essential that one make an early or at least a relatively early diagnosis, and this is extremely difficult. Pain is a rare early symptom in cases of cancer of the digestive tract, and one must look elsewhere for clues. If one looks for palpable tumor, for anemia or for marked loss of weight one will usually have waited too long. There is one and only one means that I know of; that is, to suspect any "digestive symptom," progressive or intermittent dysphagia, gastric dyspepsia, increasing constipation, alternating constipation and diarrhea, attacks of intestinal colic appearing without cause and not yielding to

symptomatic therapy, especially if associated with slight loss of weight, some loss of appetite and, perhaps most important of all, persistent traces of occult blood in the stool (for while hemorrhage is rare, constant slight bleeding is very common). These symptoms usually appear in middle or later life, but in younger persons carcinoma is not unknown, even that slowly growing form usually met with in older patients. Cancer of the digestive tract, as a rule, is of slow evolution. There must always be a long silent period, and what one believes to be the first or second act in the drama may be in reality the third or fourth.

In my opinion, the remarkable feature of neoplasm of the digestive tract is the striking rarity of a previous history of digestive disturbance, and I cannot agree with those who think that gastric carcinoma develops in most cases from achylic gastritis. In a large series that I studied, 5 per cent of the patients gave a history suggesting peptic ulcer, and less than 15 per cent had had gastric dyspepsia; more than 80 per cent had had absolutely no previous history of gastric indigestion; the condition comes "out of the blue," *"wie ein Dieb beim Nacht."* If suspicions are aroused, it is obvious that all the essential tests should be made—gastroscopic, esophagoscopic, sigmoidoscopic and thorough fluoroscopic and roentgen studies, together with examination of the blood and urine, of the stool and of the gastric and duodenal contents. In no instance of suspected pathologic change should one fail to palpate the abdomen in a hot bath or to make a digital rectal examination. From some of these studies one may get definite confirmation of one's tentative diagnosis; in other cases no information of vital importance will be obtained, but even in the latter group, if the symptoms persist, if there is occult blood in the stool and if there is loss of weight, I feel that an exploratory laparotomy is absolutely justifiable. It is frequently wiser to operate on the basis of a well grounded suspicion than to wait until a definite diagnosis can be established. On the other hand, a large growth is not necessarily inoperable. I have seen many large gastric neoplasms with no evidence of metastases to the liver or the regional lymph glands and small growths with extensive metastases. Each case must be a law unto itself. Even when complete removal is impossible, relief may frequently be obtained, not always by short circuiting but sometimes by resection.

Esophageal neoplasm, with its early obstructive symptoms, its slow rate of growth and its tendency to late metastasis, should be a favorable field for the surgeon, but the technical difficulties have so far proved insuperable. I feel confident, however, that they will be overcome, probably as a by-product of the amazing improvement in surgical treatment of the lungs and mediastinum.

In the case of the stomach, early diagnosis is most difficult because of the predilection of cancer to originate in the silent area, the lesser curvature. An increasing number of cures lasting five years or more are being reported, while in the large bowel, where early diagnosis is much more likely, the results are surprisingly good.

In the case of carcinoma of the pancreas, should one do nothing or at most advise a cholecystogastrostomy or a duodenostomy to relieve the symptoms and possibly prolong life, or should one advise resection, realizing that, although the operation is dangerous, if it is successful long life is possible with the proper diet, and with administration of insulin and possibly pancreatic extract? I am sure that pancreatic malignant disease could be diagnosed much earlier if one became "pancreas-minded," if one thought of such diseases as the possible cause of certain symptoms referable to the upper part of the abdomen, periodic attacks of persistent pain in the back for which no explanation can be found in the stomach, the duodenum, the gallbladder or the intestine. Studies of the stool and quantitative estimation of pancreatic ferments in the duodenal contents or in the stool can be of help in this connection.

The gallbladder is perhaps the most fertile field for honest controversy. There is, of course, no question that operation is the only treatment for empyema and the wisest for cholelithiasis with frequently recurring attacks of severe pain. But in other conditions there is much difference of opinion. Should one operate immediately for acute cholecystitis? Many surgeons think so and claim that the mortality is no greater than with an interval operation, but this is at variance with certain German statistics showing the mortality to be three times as great. I cannot help but feel that a waiting policy is wiser if the patient is in a hospital where he or she can be watched with scrupulous care and where there are facilities for frequent leukocyte counts.

Graham, a few years ago, said that he had not operated on an "acute gallbladder" for several years. I have had a few cases of perforation, but the all-embracing arms of the omentum have made of it only a small localized process in no wise affecting the subsequent interval operation. In the only case of bile peritonitis that I have observed for many years the condition was due to the slipping of a ligature on the cystic duct after a cholecystectomy. In the case of demonstrable but symptomless gallstones, I believe that the mortality risk of operation is far greater than that of the possibility of their causing malignant disease of the gallbladder. Cholecystectomy unquestionably is the operation of choice, but there is certainly still a place for cholecystostomy in that small group of cases in which there is evidence of marked infection in the liver and in the intrahepatic biliary tree as well, for long external drainage or a cholecystogastrostomy or cholecystoduodenostomy may be the only

means of curing these conditions, and a valuable crutch may have been removed with the cholecystectomy.

There is possibly mild hepatitis in most cases of disease of the gallbladder, and there is much evidence in favor of the view that in most cases the liver is the primary seat of infection, but in most instances this condition is unquestionably relatively slight and can be improved or even cured by the better biliary drainage following cholecystectomy and the proper postoperative care.

After cholecystectomy, however, there is always the possibility of certain sequelae—adhesions or stone or stricture of the common duct—and in certain cases these may reproduce the original, or inaugurate a new, set of symptoms. In a group of 84 private patients for whom I felt that operation on the gallbladder was indicated and on 63 of whom cholecystectomy was performed, a careful subsequent survey, in many cases by personal questioning and reexamination made by my associate, Dr. Howard, showed that 44 per cent of the patients were completely cured, 16 per cent relatively cured, 18 per cent improved and 20 per cent not improved.

Finally, what is to be done in that large group of cases in which there are vague dyspeptic symptoms and in which the diagnosis is usually made by the radiologist rather than by the clinician? There is no question that chronic cholecystitis is very prevalent. Some surgeons say that more than 50 per cent of the abdomens opened by them in older persons show definite evidence of cholecystic disease. I am quite sure that in this type of case operation should be the last resort and should be resorted to only after the failure of a long course of nonsurgical therapy. The objectives are relatively simple—to prevent reinfection as far as possible, to minimize the chance of duodenitis, to promote free biliary flow and to correct constipation. The teeth, tonsils and sinuses should be checked; careful habits of eating should be insisted on and a simple diet prescribed. There are no better methods to promote biliary drainage than the utilization of these normal physiologic stimuli, with frequent feedings, large amounts of the simple fats, butter, egg yolk and olive oil (to be avoided only if jaundice is present whether stones are present in the gallbladder or not), large amounts of soft greens and fruits and water in considerable amounts. If additional help is needed to prevent constipation, there is nothing better than a "morning saline."

In the vast majority of cases I am certain that these measures are far preferable to drainage through a duodenal tube and are equally effective. If all these measures fail, one may be obliged to call in the surgeon, but he should not be too optimistic as to the results of operation, for this is the group in which failures are many and complete successes few.

Perhaps certain other fields in the digestive tract should be mentioned in which borderline problems may arise: nonspecific ulcerative colitis; chronic amebiasis, for which cecal and appendical resection may occasionally be necessary to bring about a permanent cure; terminal ileitis, for which sooner or later operation is usually indicated, and even visceroptosis, for there are a few, fortunately a very few, surgeons who still harbor the chimeric illusion that suspending a fallen stomach or fixing a movable cecum will bring back normal function.

The cause of nonspecific ulcerative colitis is not known. There is no specific cure, and treatment is purely symptomatic. Vaccines and serums, nonspecific protein shock, various drugs given by mouth or by rectum (sulfanilamide, iodine, azochloramid, acriflavine, gentian violet, oxygen), while they occasionally cause apparent temporary improvement, have not proved curative. Treatment is purely symptomatic: general hygiene, rest, a high caloric, relatively low residue diet, in some cases with the addition of certain vitamins, iron if the patient is anemic, drugs to control the diarrhea and occasionally blood, salt, calcium or sugar given by vein or subcutaneously.

While in certain cases these conditions remain mild local problems with relatively long periods of remission, in practically all the cases of severe involvement the question of surgical treatment usually arises. What has it to offer? In the "severe fulminating cases," often associated with severe and frequent hemorrhage, one must have recourse to it, although unfortunately only too often it is unsuccessful. In cases of moderate or even severe involvement I am sure one only too frequently postpones operation too long. One hopes that each patient will be the one susceptible to the drug or serum; one hopes that the specific cure is just around the corner. And yet I am sure that if one operated earlier in certain of these cases and gave the intestine the complete rest which is the only hope of real cure, certain of the ileostomies could be closed after six, twelve, eighteen or twenty-four months with a *restitutio ad integrum* of the intestine. While apparently complete repair may take place in cases of very extensive pathologic change, in most cases too much damage has already been done to the colon, and a permanent ileostomy must be faced, with the intestine left in or a subsequent colectomy performed. Many prefer the latter. I have found that it is unnecessary in most of my cases, as the diseased intestine becomes strangely quiescent after the fecal stream has been diverted. Ileosigmoidostomy is, alas, rarely possible in cases of ulcerative colitis, for the rectum and the lower part of the sigmoid flexure are involved in the vast majority of cases, (probably well over 95 per cent).

I have tried to present briefly certain of the, to me at least, interesting borderline problems in the digestive field, problems frequently difficult

to solve, with results only too often unsuccessful or not completely satisfactory whether surgical or nonsurgical methods are employed. The surgeon, because of his brilliant success with the "acute abdomen," is somewhat too optimistic as to the results of surgical attack on the "chronic abdomen." The internist often persists far too long in medical measures which are obviously not bringing about permanent improvement, and frequently this delay makes surgical treatment, when it is decided on, more difficult and the results less satisfactory.

The surgeon's viewpoint should be physiologic as well as morphologic. He should think of function as well as form. The physician should realize that functional disturbances often have an organic basis and that the attack on the former is often unsuccessful because of his neglect of the latter. It should be obligatory for him to be present at the operation; the knowledge, pleasant or unpleasant, that this "autopsy in vivo" will bring, is always valuable and sometimes salutary. But to get the best results there should be close cooperation between the surgeon and the internist in diagnosis, in the preoperative care, in the postoperative treatment and even in the operative treatment of the patient.

DISEASES PECULIAR TO CIVILIZED MAN

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With the increased pace to which civilized man must adapt himself, there are several diseases accompanying his highly energized manner of living. Frequently the physician is called on to treat diabetes, peptic ulcer, essential hypertension, exophthalmic goiter, diseases of the coronary arteries and nervous and mental diseases. These conditions are exceedingly rare in primitive man and are uncommon in the lower ranks of civilized man. The more highly civilized man becomes, the more prevalent they seem to be.

As man has become less concerned with fighting, hunting and other predominantly physical activities and more concerned with mental activities, the characteristic mental and emotional mechanism has continued to increase relatively in size and in dominance until there are now also increasing the diseases I have mentioned, which are in large part due to overactivity of the kinetic system. Evidence indicates that the kinetic system may, by its excessive activity, interfere with the health and the function of certain other organs of the body. The "brain-adrenal-thyroid-sympathetic system" in an increasing number of cases is becoming hyperactive, establishing a state of such excessive activity as may fittingly be termed hyperkineticism. The background of these diseases is laid in the racial history of man, in man's phylogeny. It is only in this way that it has been possible to understand their causation, for other factors, such as infections, diet, climate and excessive physical work, have proved themselves inadequate of being the primary cause of these diseases.

ELIMINATION OF VARIOUS CAUSES

Infections.—The diseases peculiar to civilized man could not be due primarily to infections, for the same infections affect all races of man, as well as lower animals. There is no evidence suggesting that a specific infection causes any of these diseases in the sense in which typhoid fever and diphtheria are caused by specific bacteria. Infection plays only a secondary role.

Diet.—It can be said that diet is not a primary factor but that it plays a secondary role.

Climate.—These diseases cannot be due to altitude, to humidity or to temperature, as they appear wherever civilized man appears. However,

it is significant that they are more prevalent in the north temperate zone, where man is noted for being more active.

Physical Overwork.—If physical overwork were the prime factor in causing these diseases, then the consistently hard-working horse should have peptic ulcer, hyperthyroidism or neurocirculatory asthenia.

A hereditary predisposition played on by adverse factors in the environment or existing in a normal person under excessive strain in one case may produce hyperthyroidism, in another may pathologically sensitize the adrenal-sympathetic system and in still another may "step up" the brain to the breaking point or so facilitate the digestive mechanism in its activations and its inhibitions as to cause spastic colitis, hyperacidity, peptic ulcer or indigeston. These diseases seem to be largely due to hyperactivity of the group of organs that initiate and continue the transformation of energy. They belong to the diseases of pathologic physiology, bred in man's phylogeny, in which there is a sustained, abnormally high activity of the entire kinetic system. Thus, these mental and emotional states leading up to hyperthyroidism, neurocirculatory asthenia or peptic ulcer may be regarded as the consequence of pathologic activation of the "brain-thyroid-adrenal-sympathetic system."

NEUROCIRCULATORY ASTHENIA

During the World War a certain number of men in service at the front became incapacitated on account of a disorder which was called "soldier's heart." These patients exhibited a rapid heart beat, nervousness and fatigue. In the stress of civilian life there are observed many cases of this same disease, which is usually given the name "neurocirculatory asthenia." This disease resembles, and is often mistaken for, mild hyperthyroidism, especially in those cases in which there are a goiter and a moderate increase in the basal metabolic rate. It is a pathologic state of excessive stimulation of the adrenal–sympathetic nervous system due to changes in facilitation within that system itself or to constant thalamic stimulation, and, since other kinds of treatment have failed uniformly, my associates and I followed the results secured by the surgical treatment of hyperthyroidism and sought in selected cases of neurocirculatory asthenia to reduce by surgical measures the activity of the adrenal-sympathetic system.

This condition is most frequently found in persons in a state of worry about finances or environmental conditions grafted on a background of brilliant achievements in school and college.

Since I considered that the adrenal glands constitute the power station, or the brain, of the sympathetic system and that in the presence of neurocirculatory asthenia this power station is too active, I tested this conception in certain cases by severing the nerves emerging from the adrenal glands.

My first task was to differentiate neurocirculatory asthenia from a group of diseases which have many symptoms in common with it. I excluded the diseases analogous to it, the mechanism of which involves changes in the patient's fundamental personality, such as psychoneuroses, psychoses and constitutional inferiority; in short, I excluded all cases of patent psychic disease and limited my attack to those cases in which a pathologically excessive activity of the adrenal-sympathetic system was manifested and a classic picture of abnormal stimulation of the sympathetic nervous system was produced.

The theoretic and practical indication for denervation is found in the person whose mental and psychic mechanism acts within a normal range but whose system is under an otherwise uncontrollable stimulation analogous to that which produces hyperthyroidism or that which produces Raynaud's disease.

Neurocirculatory asthenia is more frequently found among women than among men and is essentially a disease of early adult life. The more nearly the symptoms resemble those of hyperthyroidism, the better the operative results. As with hyperthyroidism, the physical type of the patient with this condition is the slender, nonathletic type, a fact which indicates that while the kinetic system is rising the rest of the organism is declining, thus following the pattern of orthogenesis. As has been stated, patients with neurocirculatory asthenia are generally intellectually and emotionally outstanding, just as civilized man is intellectually and emotionally outstanding in comparison with primitive man.

PEPTIC ULCER

The seven biologic excitants of the adrenal-sympathetic system are pain, emotion, infection, hemorrhage, asphyxia, thyroid hormone and epinephrine. Pain certainly aggravates a peptic ulcer. Emotion and physical exertion are closely related; both aggravate peptic ulcer, as do equally the toxins of infection. The thyroid hormone my associates and I also believe to be clearly related to peptic ulcer, as we have noted cases of peptic ulcer associated with hyperthyroidism. In these cases thyroidectomy has been followed by cure not only of the hyperthyroidism but of the ulcer.

Accordingly, when there is obstruction at the pylorus it may be assumed that a healed, or at least an inactive, ulcer exists. In this case almost ideal results are secured by a simple gastroenterostomy. When there is an active nonobstructive ulcer in an active, young, high-strung, worrying person, gastroenterostomy is not indicated, because of the tendency to formation of recurrent ulcers. Recurrent ulcers are more resistant to treatment than is the primary ulcer. In the case of a recurrent, intractable ulcer in a young person with a high-strung,

worrying temperament, we seek to change the pathologic physiology by denervation of the adrenal glands; otherwise, gastric resection is the operation of choice.

DIABETES

Cannon has shown that glycosuria accompanies emotion. If the pathologically high stimulation of the pancreas by the highly charged sympathetic system in cases of hyperthyroidism contributes to or causes diabetes, the disturbed carbohydrate metabolism should be abated or cured by thyroidectomy. Dr. Henry J. John found cure or abatement of the diabetes after thyroidectomy in 55 per cent of cases in which diabetes was associated with hyperthyroidism.

ESSENTIAL HYPERTENSION AND HYPERTHYROIDISM

Essential hypertension and hyperthyroidism can perhaps best be taken up as a comparative study. Through my observation and study of the histories of patients with these conditions, I have noticed that with each there is a distinct difference in personality and that apparently there is an inherited type of physical characteristics predominant in the hypertensive patients and distinctly different from that observed in the patients with hyperthyroidism. The hypertensive patients are, in the first place, of a heavier build, usually averaging 20 to 30 pounds (9 to 13.5 Kg.) more than patients of the same height with hyperthyroidism. They have larger hearts, larger celiac ganglions, a larger trunk and an especially large chest. They are endowed with tireless energy, and, although both groups of patients have a capacity for large amounts of work, patients predisposed to hypertension have a greater capacity for *sustained* output of energy. The hypertensive person at school tends to be interested in physical work, and he is a leader in organizing teams and clubs. He is usually the student who makes a name for himself in such athletic pursuits as football, boxing and baseball, whereas the person with a hyperactive thyroid is more interested in such activities as debate, creative writing and the more esthetic subjects and displays a definitely higher scholastic ability. With this ability there is associated a more unstable, excitable type of personality, which is often in conflict with the driving ambition generated by the high degree of intelligence. The hypertensive person throughout life is able to do vast amounts of work, but unlike the person with hyperactivity of the thyroid, he is stable and constant, which aids his high intelligence in fitting him for a prominent position in business.

When one sees these two different groups of patients in the clinic, the mental and emotional variations are apparent. The hypertensive patient, who calmly discourses on his symptoms, is rarely alarmed in the least when it is suggested that he should have an operation, often

showing less concern than the surgeon. On the other hand, the patient with hyperthyroidism is so excitable and unstable that the whole hospital must be organized to keep from him the details as to when his operation is scheduled, in order to prevent the development of a thyroid crisis.

Essential Hypertension.—Barker and Graham [1] claimed that approximately 15 per cent of all adults have hypertension and that 23 per cent of patients who are more than 53 years of age die of hypertension. Ascroft,[2] from a survey in England, says that, after the age of 50, 1 death in 4 is due to arterial hypertension, and he claims further that "whatever the initial cause of raised blood pressure, in 'essential arterial hypertension' the hypertension itself is the dangerous factor and the commonest cause of death."

The racial distribution of hypertension indicates that the highest known incidence of high blood pressure is among those who struggle with the complexity of civilization. Thus, in the aboriginal native whose ceremonies protect him against social struggle, the incidence of hypertension appears to be low. On the other hand, in the urban American Negro, who has been removed for several generations from his protective aboriginal society, the incidence is higher. This seems to be true also of the recently westernized Japanese, who now appear to have a high incidence of hypertension as compared with a presumably similar stock, the calm Chinese, who have not yet been influenced by the pressure of Western civilization.

It is important to determine what levels of blood pressure should be considered hypertensive before any other steps are taken. It is generally considered that in middle-aged or young persons a systolic blood pressure of 140 to 150 mm. of mercury and a diastolic blood pressure of 90 to 95 mm. is either borderline or indicative of early hypertension. In older patients a systolic pressure of 150 mm. is usually accepted as the minimal hypertensive level.

It has been observed that the sympathetic system has an important function in the production and maintenance of high blood pressure. I have already reported that in the course of denervation of the adrenal glands and division of the splanchnic nerves if the sympathetic nerves are manipulated there is a rise in the blood pressure, both systolic and diastolic, sometimes to such a height that it cannot be measured by a manometer, while, on the other hand, if the field is first flooded with procaine hydrochloride there is no rise but rather a dramatic fall in

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the blood pressure. The adrenal-sympathetic complex is the only tissue in the body the manipulation of which can thus specifically affect the blood pressure.

On the basis of these observations my associates and I resected the celiac ganglions and broke up the sympathetic complex. It was hoped that the operative procedure based on these findings might enable us to reduce the high blood pressure of a patient with essential hypertension to normal on the operating table, and it was felt that, since postganglionic fibers cannot regenerate, there should follow a reduction in the blood pressure.

We have treated hypertension by 535 operations on 314 patients, of which 434 were celiac ganglionectomies on 260 patients. Sixty-one patients were operated on three or more years ago. The average blood pressure of the patients living at the time of this report (55 per cent) was 213 systolic and 130 diastolic on admission to the hospital; at present the average blood pressure is 187 systolic and 116 diastolic. Symptomatic relief has been experienced in 88 per cent of our total series; precordial pain has been relieved in 83 per cent, and 82 per cent of the patients have gone back to work.

Among the patients who left the hospital three or more years ago, 33.3 per cent have died after varying periods. It is generally accepted that approximately 60 per cent of patients with essential hypertension, if not operated on, die from cardiac failure. Of our series of patients on whom celiac ganglionectomies were performed, only 11.8 per cent died from cardiac failure. Also, in our whole group of patients there has not been a single "cardiac death" in the hospital following the operation.

Hyperthyroidism.—Denervation of the adrenal glands can convert a hyperplastic thyroid into a colloid goiter, thus abating the symptoms, reducing the patient to a normal state and sustaining this normal state. Since denervation can accomplish this, hyperthyroidism is not due to a dysfunction of the thyroid or to a change in the iodine molecule, nor does it originate in the thyroid itself. It is imposed on the thyroid from influences outside the gland and is not due to diet or to changes in the blood.

The curative effect on hyperthyroidism produced by adrenal denervation clearly demonstrates that the hyperthyroidism is definitely related to the brain-adrenal-sympathetic system and does not stand alone as an isolated phenomenon. It is an excessive functional or pathologic stimulation of the entire mechanism of civilized life. The background of civilization and the background of hyperthyroidism are identical, whereas among the wild and the domestic animals, among the primitive races of man and among the drifters, the morons, there is generally neither hyperthyroidism nor civilization.

Through results obtained from our research laboratory my associates and I concluded that nothing but epinephrine can cause the crisis of hyperthyroidism. It followed that if we could sever the connection between the adrenal glands and the organism, not only would this body-wide stimulation be reduced but the activity of the thyroid gland and of the brain would be diminished.

The effects of adrenal denervation in a case of hyperthyroidism may be favorably compared with those of thyroidectomy. After thyroidectomy the patient is at first extremely nervous and difficult to quiet, while after denervation, to the extent that preoperative excitation is avoided, the patient usually is calm and rests well. More sedatives are required after thyroidectomy than after adrenal denervation. After thyroidectomy the pulse rate is usually increased and remains so for several hours; after adrenal denervation the pulse rate gradually drops. Excessive perspiration is noted after thyroidectomy, and little or none occurs after adrenal denervation.

The immediate beneficial results are thus obvious; the remote results should be just as obvious, since the power of the adrenals to excite the thyroid to increased activity is permanently lessened. In our series of cases of hyperthyroidism associated with hyperplasia of the thyroid in which adrenal denervation has been performed, we have seen the entire picture of hyperthyroidism disappear promptly, the basal metabolic rate return to normal and the hyperplasia undergo transformation to the safe colloid state.

CONCLUSIONS

The diseases peculiar to civilized man would seem to be due to excessive use of those organs that through their development have distinguished civilized man from primitive man and, in turn, have distinguished primitive man from the domestic and wild animals. The real background of these diseases is the background of the power and personality of man—the brain, adrenal, thyroid, sympathetic nervous system complex, which has evolved to its highest development in civilized man. The principle is analogous to the mechanical effect of putting into an ordinary motor car an engine twice as powerful as the car was designed to handle. If the car were not used there would be no difficulties, but if in addition to having high-powered equipment it were driven excessively, as civilized man is, then complications could be expected. Civilized man has the most highly energized formula of all the animals in the world, and his life in the north temperate zone is such that he is driven at a speed as though life were a race. Consequently, pathologic physiologic change develops which may produce diseases of the coronary arteries, diabetes, peptic ulcer, hyperthyroidism or essential hypertension.

Naturally, the African native with his low energy equipment could not qualify either for civilization or for these diseases of civilized man.

An important part of treatment is clearly prevention. One may hope that some day civilized man will understand the limitations of his equipment, so that by training and education he may adapt the coming generations to the risk of these diseases. When this has developed, there will also evolve better modes of treatment. The present surgical treatment of interference with the sympathetic nervous system's influence on the thyroid gland in conditions of neurocirculatory asthenia, hypertension, hyperthyroidism etc., although as yet with an undetermined effect in some cases, is leading the way in this evolution.

REMOVAL OF LONGITUDINAL SINUS INVOLVED IN TUMORS

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There is occasionally presented to the neurosurgeon the problem of dealing with dural meningiomas that have invaded the longitudinal sinus and especially with bilateral dural tumors in which the longitudinal sinus is incorporated in the mass. Unless the affected part of the longitudinal sinus is resected there is no possibility of curing the tumor, and, in most instances, so extensively has the tumor grown to the falx and sinus that even removal of the mass with the full expectation of recurrence is well nigh impossible. When the great size of the longitudinal sinus and the numerous large tributary cortical veins entering it from both sides are considered, it is not difficult to realize that surgeons have hesitated to resect the longitudinal sinus both from fear of producing irreparable harm to such a seemingly all-important venous trunk and from the technical difficulties involved. There has been scant evidence indeed to support the thought that resection of this sinus might be tolerated, particularly in its posterior portion. Many patients with thrombosis of the longitudinal sinus have come to necropsy. But in the case of such a patient there is frequently an acute inflammatory basis, and many of the contiguous cerebral veins are also included in the process. Moreover, in many an acute septicemia coexists. It is doubtful whether experimental evidence would be pertinent, except perhaps in monkeys. In dogs there is only one cluster of cerebral veins on either side that enters the sinus, whereas in man there are many.

It is, of course, clear that in dealing with bilateral tumors and frequently even with unilateral dural tumors the longitudinal sinus is frequently occluded by the tumor either by compression or by direct invasion, so that removal of a section of the longitudinal sinus really adds little or nothing to the demand for collateral venous circulation. In these cases the venous obstruction has doubtless been gradually progressive, and because of this there has been time for the collateral circulation to develop. This condition was true in both of my cases in which the longitudinal sinus was resected posterior to the rolandic vein, and doubtless it was also true in nearly all of the cases reported in the literature. Whether a patent sinus could be similarly resected can only be conjectured; there is no evidence from the literature to support or deny such a claim.

Gradually a small number of cases of resection of the longitudinal sinus in the course of tumor extirpations have been assembled from the literature. Kenyon (1915) reported the first case in which the longitudinal sinus was doubly ligated in the frontal region, the ligatures being 2½ inches (6.3 cm.) apart. Rand (1923) was apparently the first deliberately to resect about 10 cm. of the sinus with a large bilateral dural meningioma with massive hyperostosis over it. The resected sinus was well in front of the rolandic vein. The patient made a splendid recovery with no loss of motor function, and a note from Dr. Rand on March 19, 1940, stated that the patient is well eighteen years later, an occasional epileptic attack being the only residual disturbance. In 1926 Towne removed a similar tumor weighing 428 Gm. and a section of the longitudinal sinus (length not stated), but his patient died two months later. The longitudinal sinus was filled with tumor.

David, Bissery and Brun (1935) reported a case in which operation was done by Vincent of Paris, France. A bilateral tumor—12 Gm. on the left and 18 Gm. on the right—was removed with 5 or 6 cm. of longitudinal sinus just in front of the rolandic vein. The result was excellent, with no motor loss. No note was made of the patency or occlusion of the longitudinal sinus. Horrax has successfully removed sections of the longitudinal sinus in 2 cases, 1 (1931) included in Cushing's book on meningiomas (6 cm. of sinus in front of the rolandic vein was resected) and another, reported by Maltby (1939), in which 4 cm. of the sinus posterior to the rolandic vein was excised. The patients in both cases made excellent recoveries, with slight but gradually diminishing spasticity of the extremity. In Horrax' second case resection was done in a single operation, doubtless because his earlier experience had given him a greater sense of security concerning removal of a section of longitudinal sinus. In all the preceding cases the sinus had been resected after recurrence or in stages for tumors of excessive size and vascularity. In Horrax' second case (Maltby) a prolongation of the tumor was drawn out of and doubtless occluded the longitudinal sinus. Rowe (1939) reported another splendid result, with a large bilateral dural tumor with hyperostosis, together with which 6 cm. of the longitudinal sinus was resected. A letter from Dr. Rowe stated that he has since been unable to locate the patient and that the patency or occlusion of the sinus was not investigated.

Two remarkable cases (Davidoff [1937] and Tönnis [1935]) complete the series of cases of resection of the longitudinal sinus that I have been able to assemble from the literature—a total, therefore, of 9 (in Kenyon's case ligation, not resection, was done). The operation in all except Towne's case was successful, without any disturbances attributable to resection of the sinus, and Towne's patient lived over two months. Most of these patients had some degree of temporary

spasticity of the lower extremities after operation, but this was clearly due to trauma of the motor cortex incident to extirpation of the growth and not to any effects of removal of the longitudinal sinus.

Davidoff's case and also that of Tönnis give evidence of the very highest surgical skill, as indeed do all the others, for such operations are no mean feats. Davidoff's tumor, removed in three stages, weighed 835 Gm. and was perhaps the largest cranial tumor to have been successfully removed. The hyperostosis and contained tumor weighed 270 Gm., and the intracranial portion, 565 Gm.! The length of sinus removed is not stated. A letter from Dr. Davidoff (Jan. 22, 1940) states that, although the patient has some slight spasticity on the right and a slightly hesitant speech, she is quite well and does her own housework.

Tönnis removed not only a section of the longitudinal sinus (length not stated) but part of one transverse sinus and the tentorium, through which the tumor had penetrated into the posterior cranial fossa. And his patient recovered with no defects except homonymous hemianopia.

To the aforementioned group of cases 4 of my own are added. In 2, resection was done in the anteriormost part of the sinus, and in 2, posterior to the rolandic vein. In 2 of the cases the sinus was excised when the tumor had recurred, and in 2 the sinus was removed at the first operation, when the tumor was known to be bilateral.

REPORT OF CASES

Case 1.—C. W. L., a white man aged 49, was admitted to the hospital because of headache and a "change of disposition." A cerebral injection of air was performed May 7, 1927. This showed a tumor in the left frontal lobe. An exploration was made May 8, and a small dural tumor, weighing 27 Gm., was removed from the anterior portion of the falx. The tumor was thought to be a dural meningioma. The patient made a complete recovery, and his headache and mental symptoms entirely disappeared.

Four months later he reentered the hospital because his original symptoms had returned. The wound was reopened, and a recurrent tumor weighing 20.6 Gm. was shelled out with the finger. It was realized that this could not be a permanent cure, and two and one-half weeks later (September 20) the wound was reopened and the bone removed over the longitudinal sinus and to some distance on the right side. There were no veins entering the longitudinal sinus on the right side. Clamps were placed across the longitudinal sinus anteriorly, and the sinus was divided. The incision was carried through the longitudinal sinus, and the inferior longitudinal sinus was clipped and divided. The longitudinal sinus was then divided and transfixed even with the posterior margin of the bony defect, and the entire intervening part of the longitudinal sinus and the falx were removed. The remaining ends of the longitudinal sinus were then transfixed with medium silk. The amount of longitudinal sinus removed was 8 cm.; this was well in front of the rolandic area, the posterior ligature in the sinus being about 4 cm. anterior to the rolandic vein (fig. 1).

The patient had no after-effects from ligation of the sinus. He recovered completely but returned again seven months later because of recurrence, which was evident from the protrusion at the site of the removal of bone. There was such an extensive return of the tumor that no attempt was made to remove it. The patient died three months later, June 27, 1928.

Autopsy showed massive recurrence of the tumor. No note was made concerning thrombosis of the remaining part of the longitudinal sinus. It was noted that 3 cm. of the longitudinal sinus remained anterior to the ligature in the longitudinal sinus.

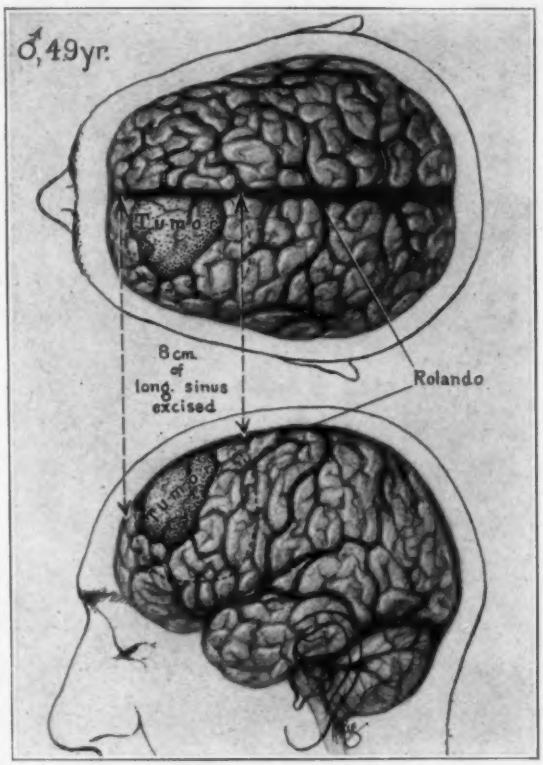

Fig. 1 (case 1).—Sketch to show the position of the tumor and the relative amount of longitudinal sinus removed anterior to the fissure of Rolando.

CASE 2.—F. R., a white woman aged 40, had observed a swelling of the forehead for the past twenty-three years; it had been steadily progressing (fig. 2). There had been headache and pain over both frontal regions for the past two years and exophthalmos of the right eye over the same period; this, too, had been steadily progressing. Roentgenograms showed tremendous hyperostosis of the frontal bones (fig. 3).

Operation.—On Nov. 21, 1936, a large sweeping curved incision was made across the frontal region, just under the hair line; it was directed posteriorly and extended from one temporal region to the other. A flap of galea and skin was

thrown forward to the supraorbital ridges. The tumor had eroded through the bone on the right side over a considerable area, but the surface was intact. The bone was so thick that several burr openings were made, and the intervening

Fig. 2 (case 2).—Preoperative and postoperative photographs of the patient. The tumor was a bilateral dural endothelioma with tremendous hyperostosis. The tumor had broken through the roof of the orbit on the right side. In the postoperative photograph the patient has concealed the marked frontal depression with her hair.

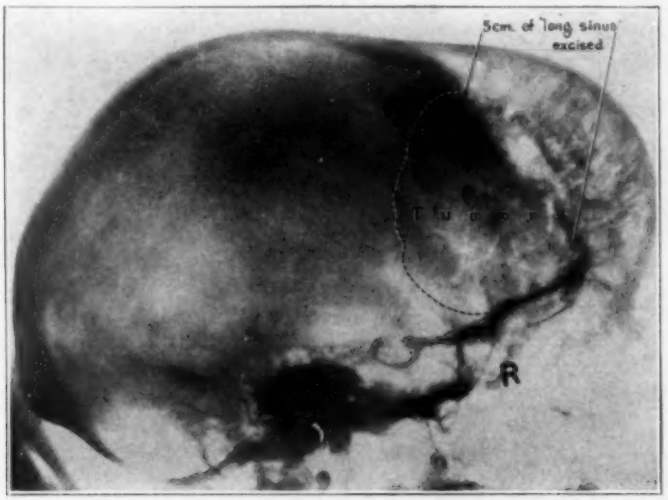

Fig. 3 (case 2).—Roentgenogram showing tremendous hyperostosis over a bilateral dural tumor.

bone was cut with large biting forceps. When the bone was turned back and broken across at the supraorbital region the tumor came out with it. It was a large bilateral dural growth (fig. 4). The sinus tore across at the posterior margin of the bone, but it bled very litttle. The mass in the orbit had broken

off from the main growth and was shelled out separately. Several veins crossing from the anterior lobe to the longitudinal sinus were coagulated with the electrocautery. The tumor mass with the overlying bone weighed 296 Gm.

The patient made an uneventful recovery and has been well to date (March 10, 1940). She is constantly employed at full time (fig. 2).

The length of sinus removed was about 8 cm.

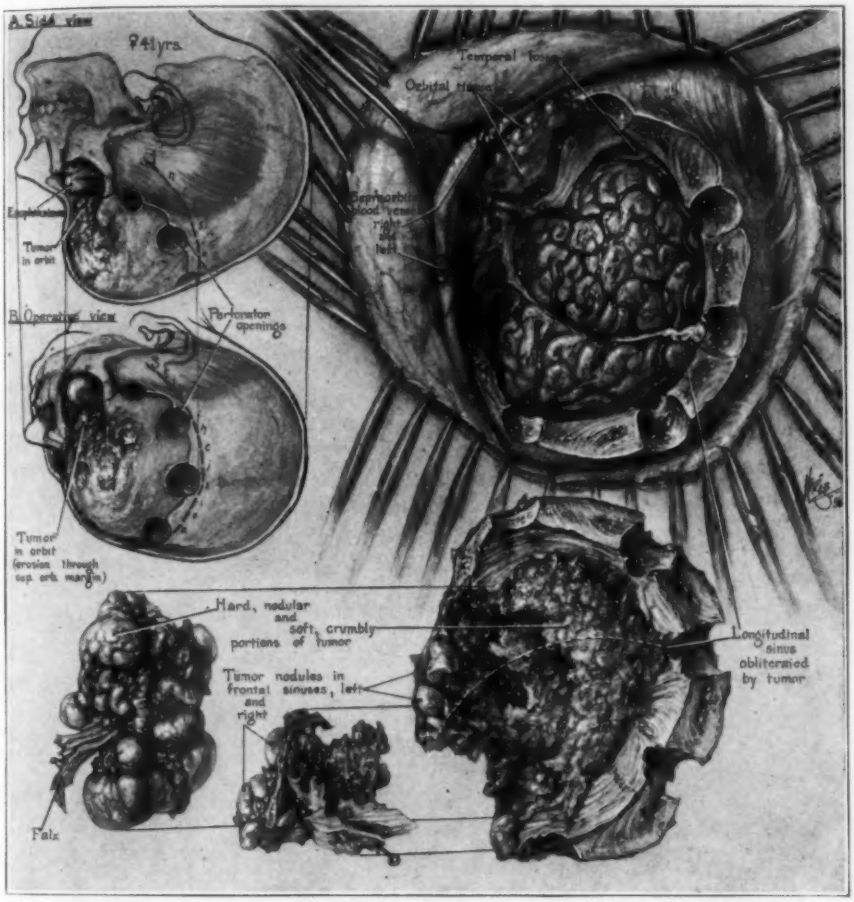

Fig. 4 (case 2).—Operative sketch showing the tumor removed and the amount of longitudinal sinus resected.

Case 3.—J. W., a man 22 years of age, consulted me May 21, 1939, because of a prominent swelling over the vertex of the skull. He had had headaches for three or four years, and for the past five months these had become more persistent and more severe, occurring almost daily and lasting from a few minutes to a few hours; they were bilateral and biparietal. The lump on the head was steadily increasing but was not tender (fig. 5). His work in college had gradually declined, and during the past year he had barely made passing grades. Concen-

tration was difficult; his memory was poor, and there had been some difficulty in getting out words and phrases, although he knew them well. On some occasions there had been transitory attacks of blurred vision. On a few occasions he had had cramps in the right leg but not a convulsion.

Neurologic examination showed slight but definite papilledema, with fulness and tortuosity of the retinal veins. The grip of the right hand was slightly weaker than that of the left. During the examination he had a cramp which drew up the right leg severely, and it was very painful. There was slight hypoesthesia in the right arm and leg; the station and gait were not affected. The patient's speech was halting; reading was stumbling but correctly done, but it seemed difficult to get the context of what he was reading. The Wassermann reaction of the blood was negative. Roentgen examination showed marked hyperostosis at

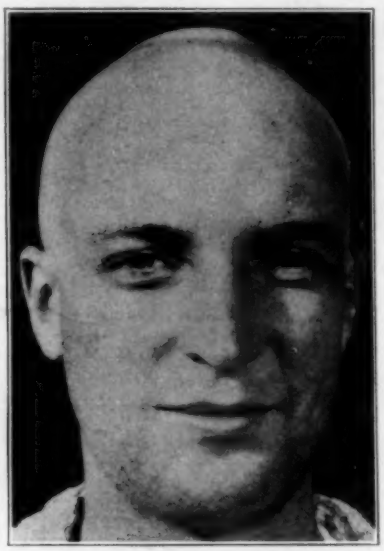

Fig. 5 (case 3).—Photograph of the patient, showing marked hyperostosis in the parietal region.

the vertex, about equal on both sides of the midline (fig. 6). The protrusion was about 1 inch (2.5 cm.) above the normal level of the scalp; it was diffuse and even.

Operation.—On May 23 a long midline incision was made over the tumor and extending well beyond it anteriorly and posteriorly. The galea and skin were then retracted; this exposed the hyperostosis, which was not very vascular. Several burr openings were made in a circle just beyond the hyperostosis, where the bone was nearly normal. With the Gigli saw these openings were connected, and the mass of bone was lifted off the dura and longitudinal sinus. As the bone was being elevated, the tumor could be seen projecting into a deep concavity in the inferior surface of the bone; it was firmly attached to it. By gradually elevating the bone flap and inserting the finger beneath it the tumor was stripped from the concavity in the bone (fig. 7). There was very little bleeding from the exposed dura and tumor; application of the electrocautery controlled this. The concavity in the bone was about 2 inches (5 cm.) long and 1¼ inches (3.1 cm.) wide. The

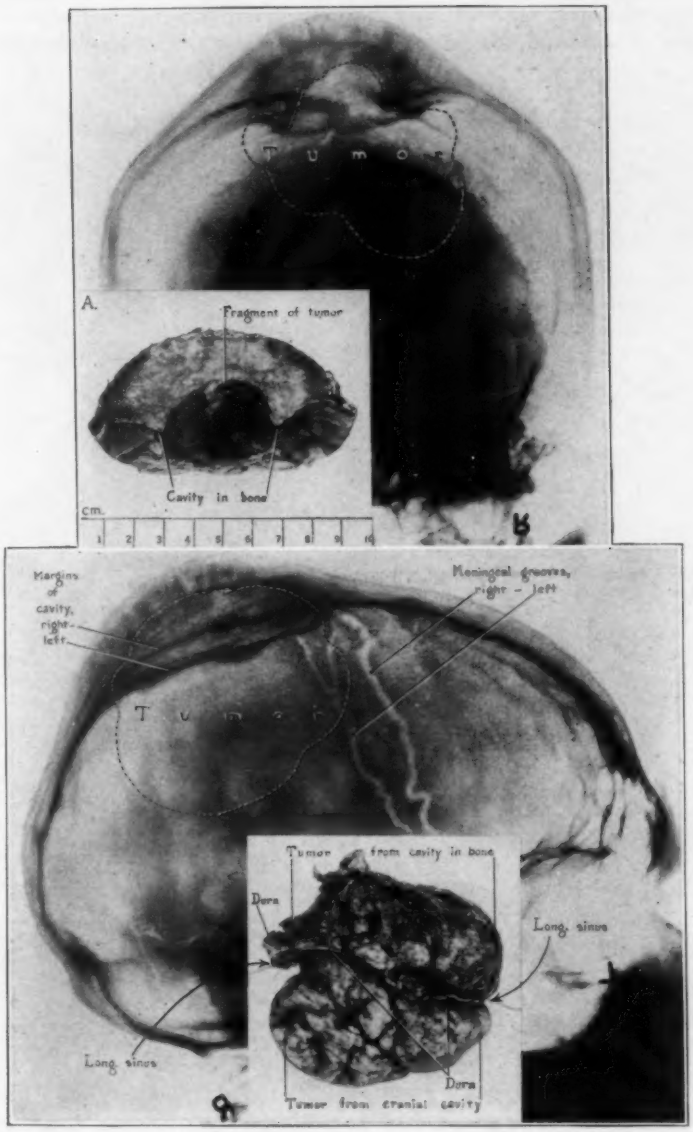

Fig. 6 (case 3).—Lateral and anteroposterior roentgenograms of the skull. The marked hyperostosis is shown, and the relative size and position of the tumor are indicated by the dotted lines. The inset in the anteroposterior view shows the section of bone removed with a large piece of the tumor in the excavation on the inferior surface. The inset in the lateral view is a photograph of the tumor and shows the longitudinal sinus, which had been completely obliterated by the tumor.

tumor was entirely on the left side of the longitudinal sinus, which was pushed in a curve to the right. The wound was closed without drainage.

The weight of the bone was 159.1 Gm.

The second stage operation was performed on June 3, ten days after the first operation. The wound was reopened; there was some necrosis on the surface of

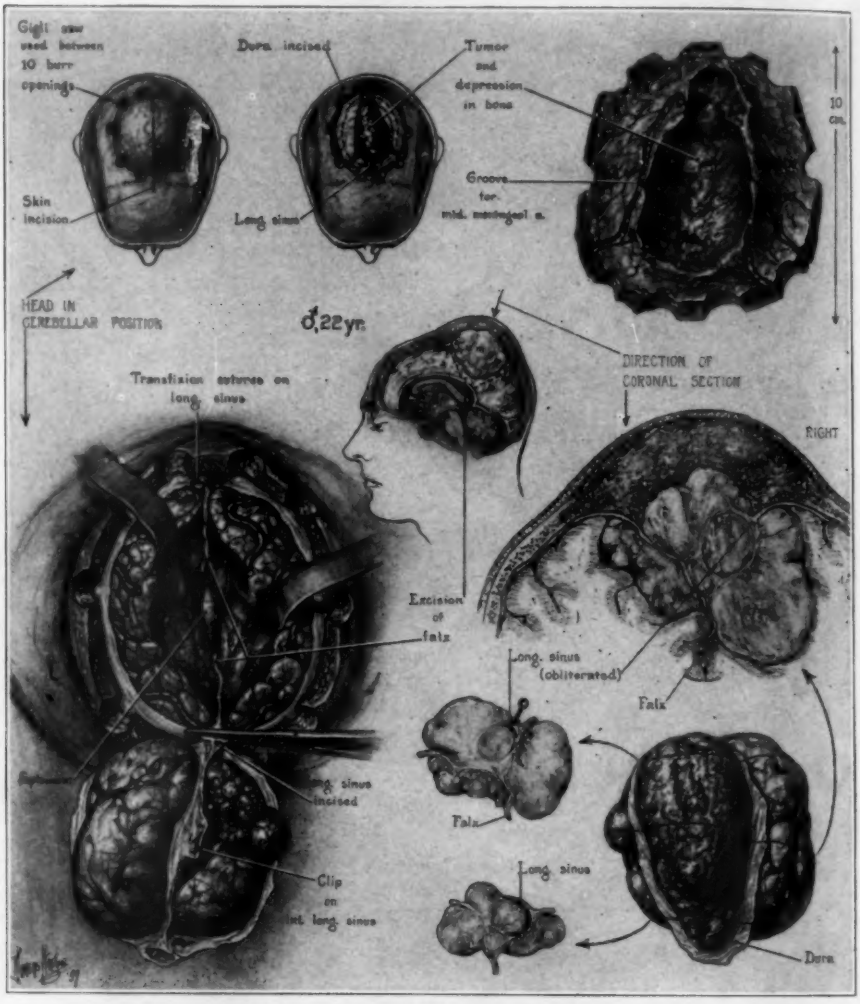

Fig. 7 (case 3).—Operative sketch showing the bone removed, the excavation of the hyperostosed bone, the position and character of the tumor and the effect on the longitudinal sinus. The operative view of the removal of the tumor and the longitudinal sinus is shown in the larger sketch on the left.

the exposed tumor. The dura was first opened in a semicircle on the right side, the termini being at the border of the longitudinal sinus. The tumor was then seen pushing the cerebral hemisphere to the right. It was a large, hard growth and was

clearly a dural meningioma. It extended deeply along the falx. The dura was then opened on the left side in a similar fashion, and the incision extended to the longitudinal sinus. The longitudinal sinus was then doubly clamped at both ends and just at the margins of the large defect in the skull. The sinus was then cut between the clamps, and the ends were transfixed with sutures of medium silk (fig. 7). Several veins entering the longitudinal sinus from the hemispheres

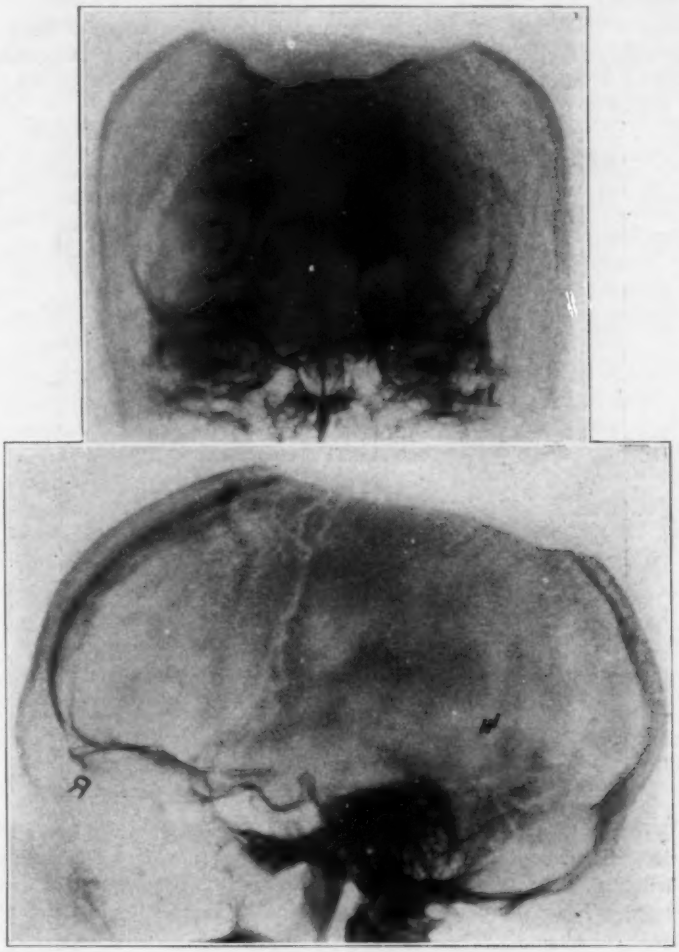

Fig. 8 (case 3).—Postoperative roentgenograms showing the amount of bone removed and the position of the silver clips placed on the inferior longitudinal sinus near its entrance into the great vein of Galen.

were thrombosed with the electrocautery and divided. These veins included the rolandic veins on both sides. About eight veins were thrombosed on the two sides; all of them were very tortuous. The falx was then divided through its entire length, including the inferior longitudinal sinus at both ends. The clips shown in the roentgenograms were on the posterior part of the longitudinal sinus (fig. 8). After the falx had been cut through at both ends the tumor was gently

shelled away from both hemispheres; it protruded far out on both sides, undermining the hemispheres, but much more on the left. On the right side it was necessary to cut away a small slice of the attached leg center to the depth of about 2 cm. and about 1 cm. in thickness. This was necessary because the tumor was adherent to the brain at this point. The tumor was bulging far out on both sides in the depths of the brain, but it was easily separated from it, with very slight trauma; the bulge was greater to the left. Little bleeding attended extirpation of this mass. A piece of fascia lata was removed from the right leg and carefully sutured to the dural margins, completely covering the entire dural defect. The wound was closed without drainage.

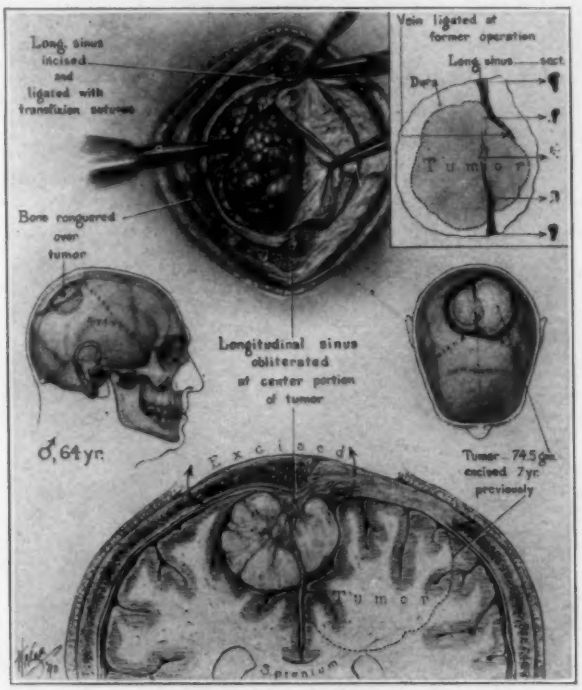

Fig. 9 (case 4).—Operative sketch of removal of the tumor. It was a bilateral dural endothelioma over which there was slight hyperostosis. The position and relative length of the resected longitudinal sinus and the relative size of the tumor are indicated. The longitudinal sinus had been obliterated by the tumor for a distance of 3 cm. at the center of the tumor.

The tumor weighed 170.3 Gm. The total weight of the bony growth and the bilateral tumor was 329.4 Gm.

The patient was conscious soon after the operation and moved both legs and arms freely. Later in the afternoon he was unable to move either leg. The first movement in the left leg began six days later, and slight movement in the right leg began on the following day. There was also diminished sensation in the legs during this period, but on the day before the motor function began to return he noticed increased feeling in both legs.

Microscopic section of the bone showed typical dural meningioma cells, and sections of the tumor showed typical dural meningioma with whorls of fibrous tissue. The longitudinal sinus was totally occluded over about three-fourths of the removed portion. The length of the longitudinal sinus was determined at the time of operation and was 12.5 cm.

Subsequent Course.—The patient's motor function steadily improved. He left the hospital June 18, thirteen days after the last operation. At that time the power was not sufficient to support him, but during the summer months he improved rapidly, and when I last saw him (Jan. 20, 1940) he was walking with very slight disturbance of gait; the two legs were equally good. He had just returned to college for the second semester; he was keen and alert and said he felt that he had completely returned to his normal mental state. The wound was soft and sunken, and there was no evidence of recurrence.

Case 4.—L. P., a white man aged 56, was operated on May 6, 1933. A dural endothelioma was removed from the falx on the left side, in the postrolandic area. The symptoms of the tumor were convulsions beginning in the right leg and weakness of the right leg. The tumor removed at this time weighed 63 Gm.

Four and one-half years later (Jan. 7, 1938) a recurrent tumor was removed from the same side; it weighed 12 Gm. The patient had slight motor disturbance in the right leg following this operation, but he walked well.

On Jan. 17, 1940, he returned because of a similar weakness in the left leg. It was clear that he had a similar tumor on the right side of the falx. He was again operated on (January 23), and a tumor weighing 35 Gm. was removed from the right side, together with the intervening longitudinal sinus and falx (fig. 9). There was no recurrence on the left side. The length of resected longitudinal sinus was 6.5 cm. and extended backward from a point about 2 cm. posterior to the rolandic vein. Five centimeters of this had been completely obliterated by the tumor, which had grown directly through it.

The patient had no increase in motor weakness following removal of the sinus and tumor. On the day after the operation his general condition was as good as before the operation. There were no noticeable effects from extirpation of the longitudinal sinus, and none could be expected, because the sinus had been completely obliterated by the tumor. He left the hospital two weeks later.

The postoperative course was uneventful.

SUMMARY

In none of the 4 cases was there any motor, sensory or other loss that could be attributed to removal of the longitudinal sinus.

The length of the longitudinal sinus removed was 5 cm. and 8 cm., respectively, in the 2 cases in which resection was anterior to the rolandic vein and 6.5 cm. and 10 cm., respectively, in the 2 cases in which resection was posterior to the rolandic vein.

In 3 cases and probably in the fourth the longitudinal sinus was already obliterated over much of the excised portion owing to compression or actual invasion by the tumor. There is as yet no available evidence by which it can be known whether the longitudinal sinus can be removed in part before gradually progressive occlusion has occurred.

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SOME ETIOLOGIC AND PATHOLOGIC FACTORS IN CANCER OF THE LARGE BOWEL

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CHICAGO

The object of this paper is to call attention to the frequency of occurrence and the histologic structure of supposedly benign polypoid growths originating in the large bowel and to present some evidence of their relation to cancer of the large bowel. Studies of these various factors have been made on material covering 200 resected cancers of the large bowel in over 300 patients on whom I have personally operated for that lesion and on 100 additional specimens of supposedly benign polyps of the colon and rectum.

The incidence of mucous polyps of the large bowel varies considerably, depending on whether they are discovered as a result of examination of patients complaining of significant symptoms or whether their frequency is noted as a result of routine postmortem examination. Even the latter approach is not ideal unless a meticulous examination of the entire area of the large bowel is carried out, for these polyps in many instances are small and hidden between the folds of mucosa. Fortunately, such a thoroughgoing search was made in 1,800 consecutive autopsies by Feyrter [1] in 1929. He observed 1,017 polyps in 1,110 of the colons examined. In discussing such observations it is important to attempt to designate which of the lesions are true tumors and which are simple hyperplasias on a senile or an inflammatory basis. This is extremely difficult to do, as many of these lesions blend one into the other, with minor histologic differences. Several gross and histologic divisions of these lesions can be made, however, and at the outset it would seem advisable to make them.

One of the most common deviations from the normal in the mucosa of the colon is the occurrence of millet seed–sized flat elevations, which are usually multiple and occur mostly in old persons, in whom they may be but another example of the hyperplasias occurring on a senile basis in other parts of the body—for example, the skin. They also occur as an inflammatory lesion; for instance, on the mucosa of a colostomy stoma. They are also commonly seen as multiple lesions in the mucosa of the bowel 3 to 6 inches (7.6 to 15.2 cm.) above or below an ulcerating

1. Feyrter, F.: Zur Lehre von der Polypenbildung im menschlichen Darm, Wien. med. Wchnschr. **79**:338-342 (March 9) 1929.

carcinoma of the bowel. Because of this position contiguous to a carcinoma it has been argued that the carcinoma may have sprung from such areas showing a tendency to growth. It could be stated equally well that they are inflammatory in origin and consist of inflammatory hyperplasia of the mucosa resulting from a reaction to the infection and irritation from broken-down tumor tissue in their immediate vicinity. The histologic structure of these minute lesions shows them in the main to be simple hyperplasias with inflammation or lymphatic hyperplasia of

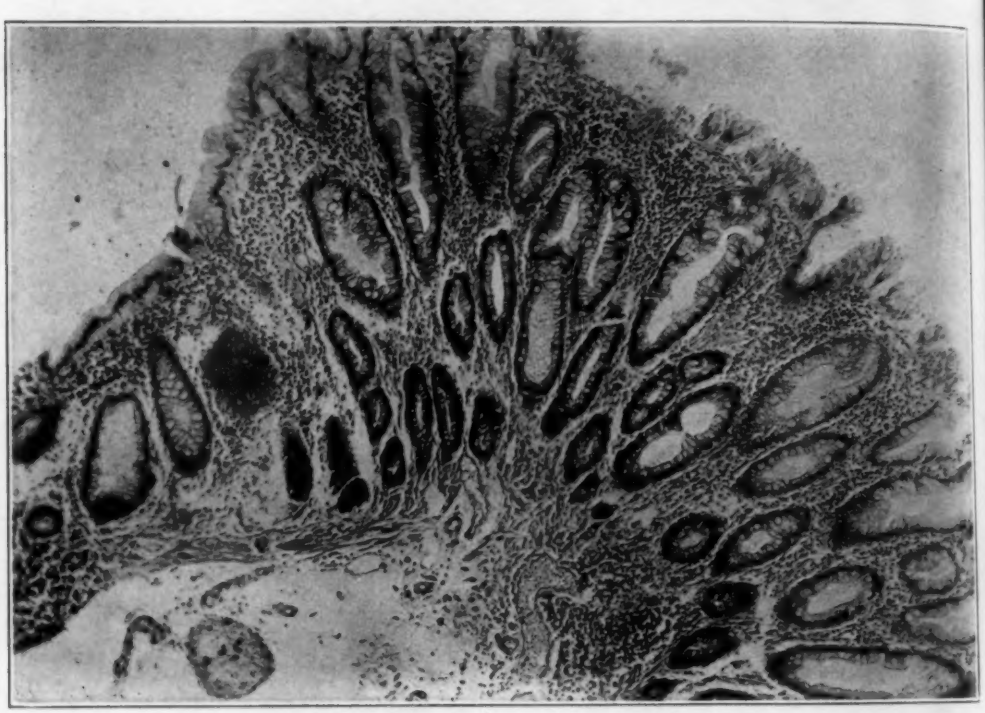

Fig. 1.—Two millimeter elevation of the mucosa near a carcinoma of the rectum, showing hyperplasia of the epithelium and inflammatory exudate between the tubules. Similar lesions appear on colostomy stomas.

the submucosa. The glandular structures of the mucosa are enlarged. The tubules of the mucosa are increased in length and have a slight tendency to branch, but the staining properties of the cells are those of the surrounding mucosa, and the relation of the cells of the tubules to the basement membrane is everywhere preserved (fig. 1). However, in exceptional instances the cells of the lesions may take on deeper staining properties, the tubules may be branching and the general appearance of the lesion may closely resemble that of larger polyps which are almost certainly tumor and not simple hyperplasia.

The lesion in figure 2 appeared on the exposed mucosa of a colostomy stoma several weeks after the colostomy was performed. In this group of small elevations of the intestinal mucosa it is not easy to differentiate hyperplasia, senile or inflammatory, and tumor growth. In Feyrter's series, 762 of the lesions found were of this type.

The next type of polyp frequently seen is the adenomatous polyp. This lesion varies in size from that of a pea to that of a large cherry and

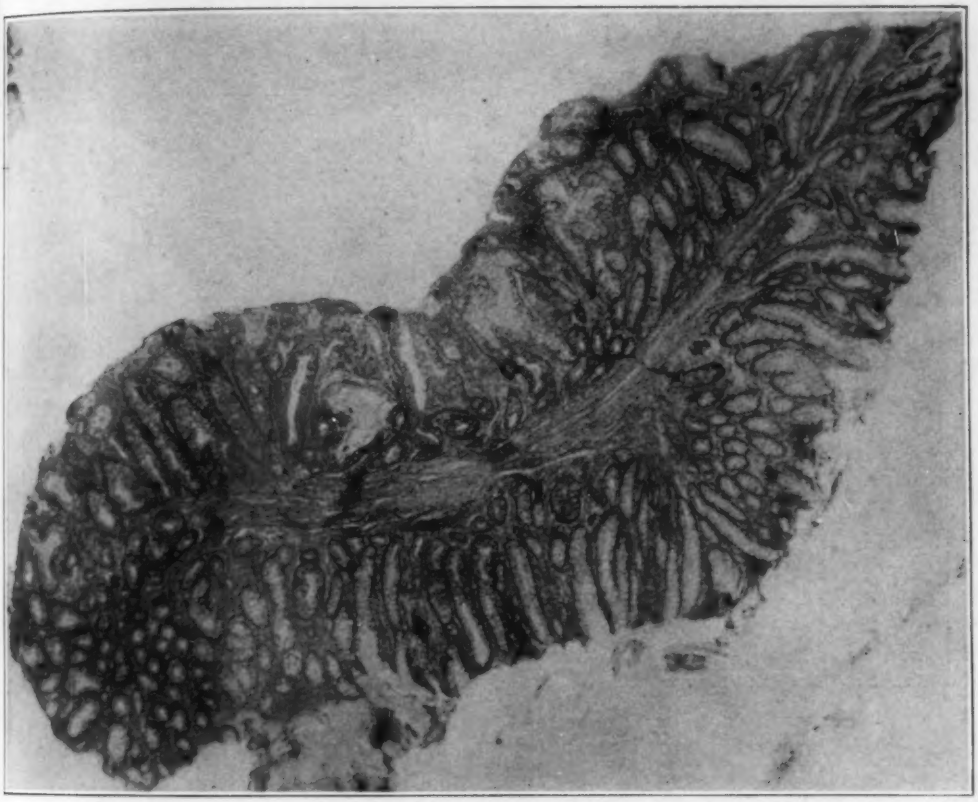

Fig. 2.—Hyperplastic nodule which developed on the mucosa of a colostomy opening. Note the branching tubules which resemble adenoma.

may have a sessile attachment, especially when small, or a pedicle when larger, due to stretching and pulling on its attachment by the peristaltic action of the bowel in its attempt to propel it along with the rest of the intestinal contents. The lesion may be transparent and of the same color as the mucosa, in which instance its histologic structure is more akin to the normal mucosa of the bowel in that the epithelial covering of the polyp is more like a hyperplasia, the cells having but little differ-

ent staining properties from normal epithelium and the body of the polyp containing sparse epithelial elements, many of which are cystic. The stroma surrounding these cystic dilatations of the tubules may have considerable round cell infiltration or inflammatory exudate. This type of polyp is the one most commonly found in children and may have a pedicle of normal mucosa 2 to 3 inches (5 to 7.5 cm.) long. This same type of lesion is found in adults and has all the indications of being a benign lesion, with little tendency to rapidity of growth or loss of differentiation of the epithelial elements (fig. 3).

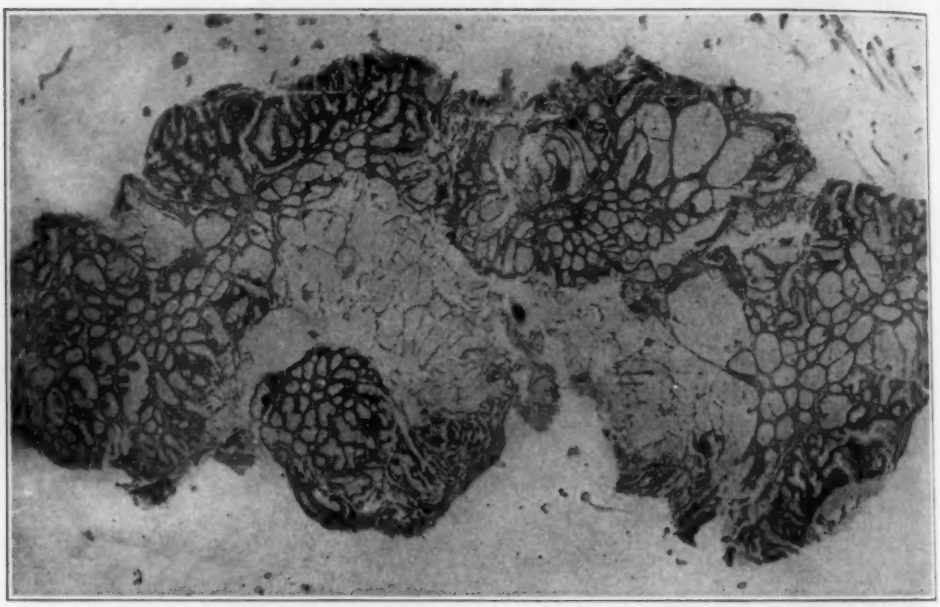

Fig. 3.—Pedunculated adenoma of the rectum. The structure is simple, but there is definite tumor formation.

Almost insensibly changing in structure are other polyps of this adenomatous group which have every evidence of a growth or tumor change in their epithelium (fig. 4, top). The color of these polyps is plum or cherry. The staining properties of the cells are strikingly different in that the protoplasm stains more deeply, as does the nuclear substance, in which mitotic figures are not common. The layers of cells in the tubules are increased in number. At the base of the adenoma the structure of the tubules is more nearly normal than at the periphery of the lesion, where branching of the tubules and cuplike enlargement of the glands take place, and a beginning loss of order of the epithelium in relation to the connective tissue pedicle of the polyp is observed.

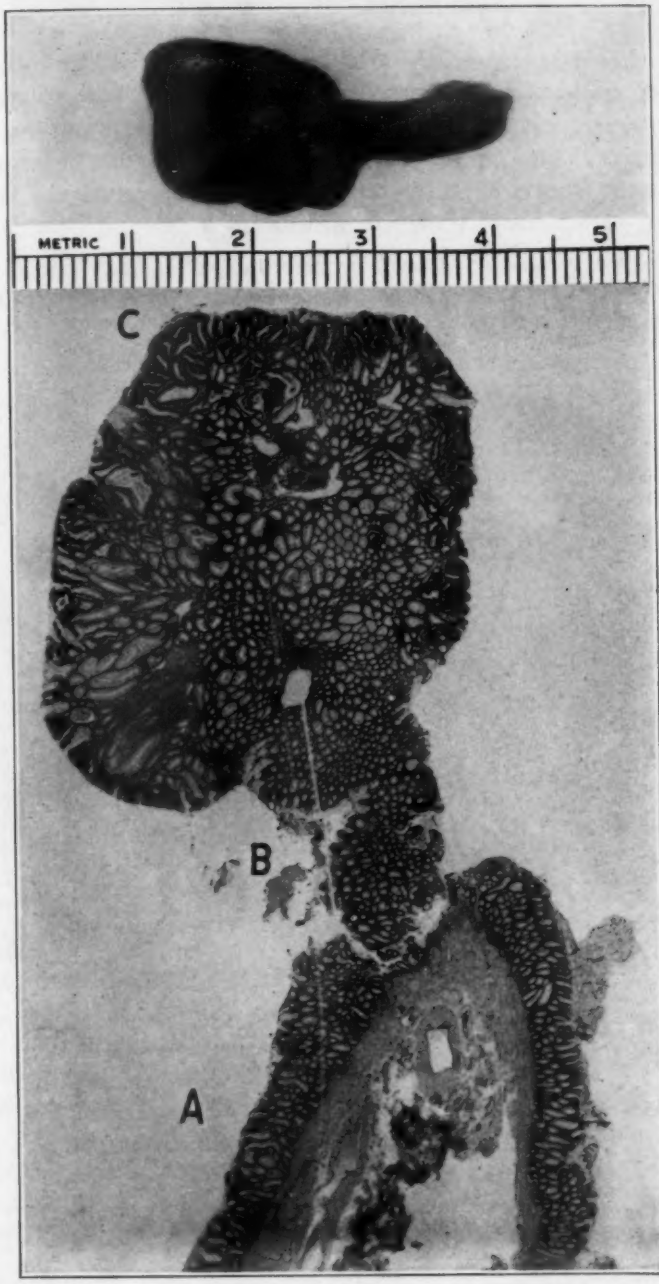

Fig. 4.—Top, pedunculated adenoma of the colon. There is a pedicle of normal mucosa. The tumor is lobulated. Bottom, pedunculated adenoma of the colon. *A*, normal intestinal mucosa; *B*, pedicle of normal mucosa; *C*, branching tubules in the periphery of the tumor, showing loss of orderly arrangement and deeply staining cells and nuclei.

In these lesions, however, the relation of the epithelial elements to the basement membrane is everywhere preserved. These polyps may become large, with a cauliflower surface, and contain branching stalks of connective tissue (fig. 4, bottom). It is easy to see that in this type of adenoma the mucosa has taken on real growth propensities and that one is dealing with a tumor benign in structure.

Westhues [2] has well described, and, I believe, with reason, a still more advanced tissue change in these adenomas, which brings their structure closer to that of a carcinoma. In these adenomas nearly all

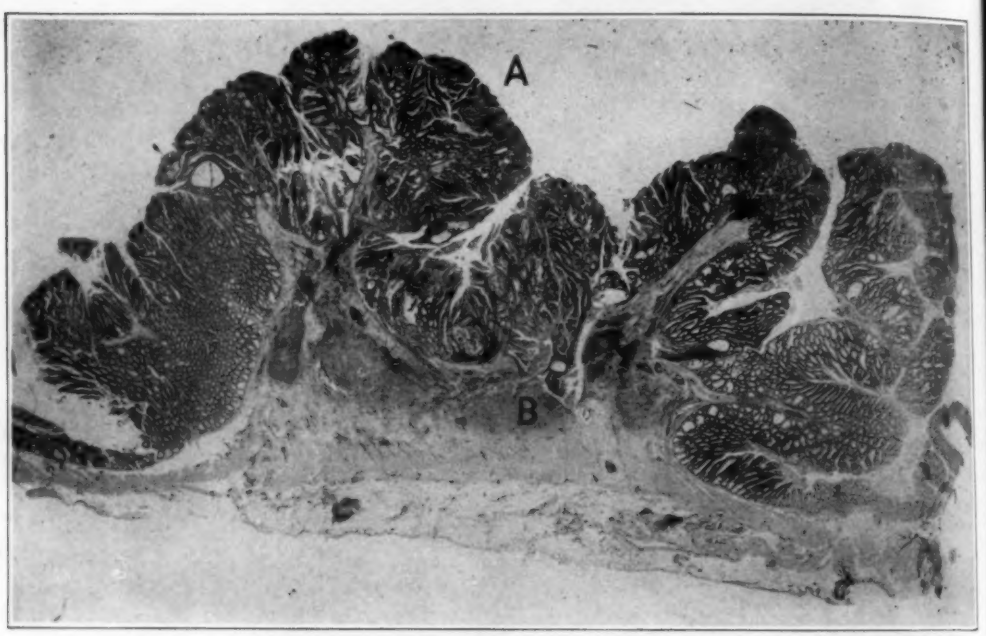

Fig. 5.—Flat adenoma of the sigmoid flexure of the colon, with complicated epithelial structure (*A*) and loss of muscularis mucosa in some areas (*B*).

order in the epithelial structure is lost. The branching, elongated tubules with cuplike outgrowths, the cells of which are many layered and deeply staining, have lost a definite relation to the basement membrane. The muscularis mucosa is absent in many places rather than broken through, and the connective tissue pedicle is sparse or absent in many places. At the base of the lesion the glandular tubules are distorted and pushed apart (fig. 5). It is but a step from this structure to actual infiltration and invasion, which, in my opinion, must still be

2. Westhues, H.: Die pathologisch-anatomischen Grundlagen der Chirurgie des Rektumkarzinoms, Leipzig, Georg Thieme, 1934.

the criterion for a diagnosis of malignant disease. It becomes increasingly apparent how difficult it is for a diagnosis to be made from a small piece of tissue taken for biopsy. The general structure of the epithelial elements may be determined and the growth tendency appreciated, but in this type of lesion the gross appearance and physical characteristics of the lesion should be correlated with the histologic structure, for the reason that any evidence of ulceration or induration of the lesion speaks volumes in favor of malignant degeneration.

Another gross division of benign polypoid tumors of the large bowel is that of papillomas or villous tumors. The tumors vary in size from arborescent stalks with the gross appearance of waving, delicate vegetation to large, flatly attached soft tumors the size of an adult fist, almost

Fig. 6.—Lobulated villous papilloma of the rectum.

occluding the lumen of the bowel (figs. 6 and 7). The average size is perhaps 2 to 3 inches (5 to 7.6 cm.) above the surface of the bowel. The tumor is very soft, and its color usually resembles that of the normal mucosa surrounding it. When immersed in water the waving, arborescent structure of the tumor is usually apparent. The tumors appear only in adults, as far as I know, and they grow slowly. Rarely they may serve as the apex of an intussusception (fig. 8). In 1 of my patients an acute obstruction of the descending colon was produced, but in most patients the tumors make their presence known by hemorrhage, sometimes acute and massive, and by the passage of tremendous amounts of mucus due to the rich development of goblet cells in their structure.

Histologically the structure of the tumor is villous, the elongated branching tubules showing increased cell layers, increased nuclear staining with some mitotic figures and a large increase of the goblet cells of the mucosa (fig. 7). Everywhere the relation of the mucosa to the

basement membrane is preserved, and the connective tissue stalk is regular and often runs out into the larger elevations of the tumor. In most of the papillomas adenomatous structures are found at the base

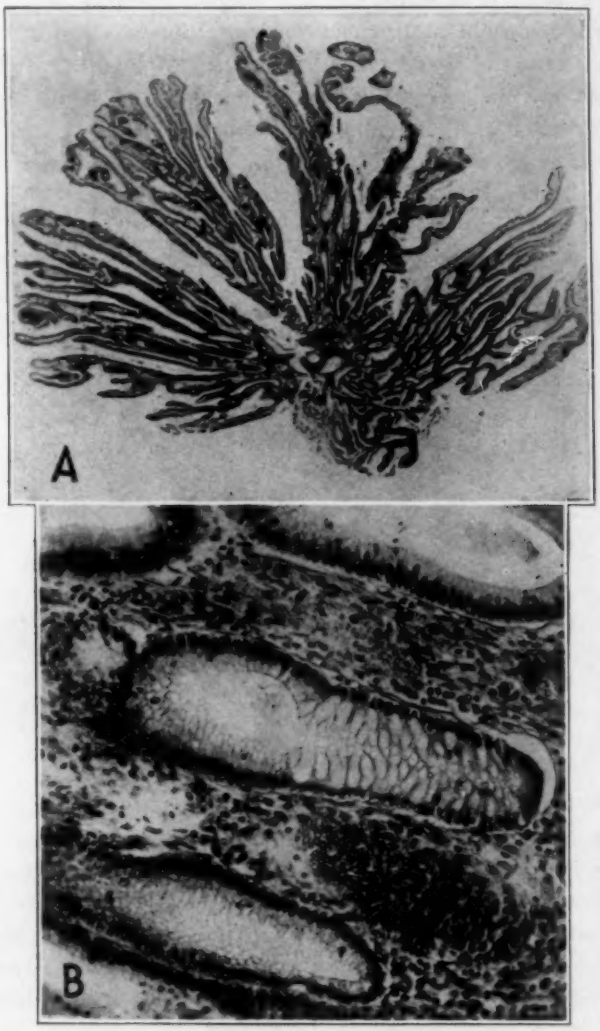

Fig. 7.—*A*, photomicrograph of the villous structure of tumor shown in figure 6. *B*, high power magnification of the tubules of a villous tumor of the colon, showing increased cell layers, increased goblet cells and mitoses but regular and orderly arrangement of the epithelium in relation to the basement membrane.

of the tumor, some of which are cystic. The tendency to wild, disorganized tissue growth is also found in these tumors, and in 2 of 27 cases I have seen an early carcinoma beginning in the lesion. Many of

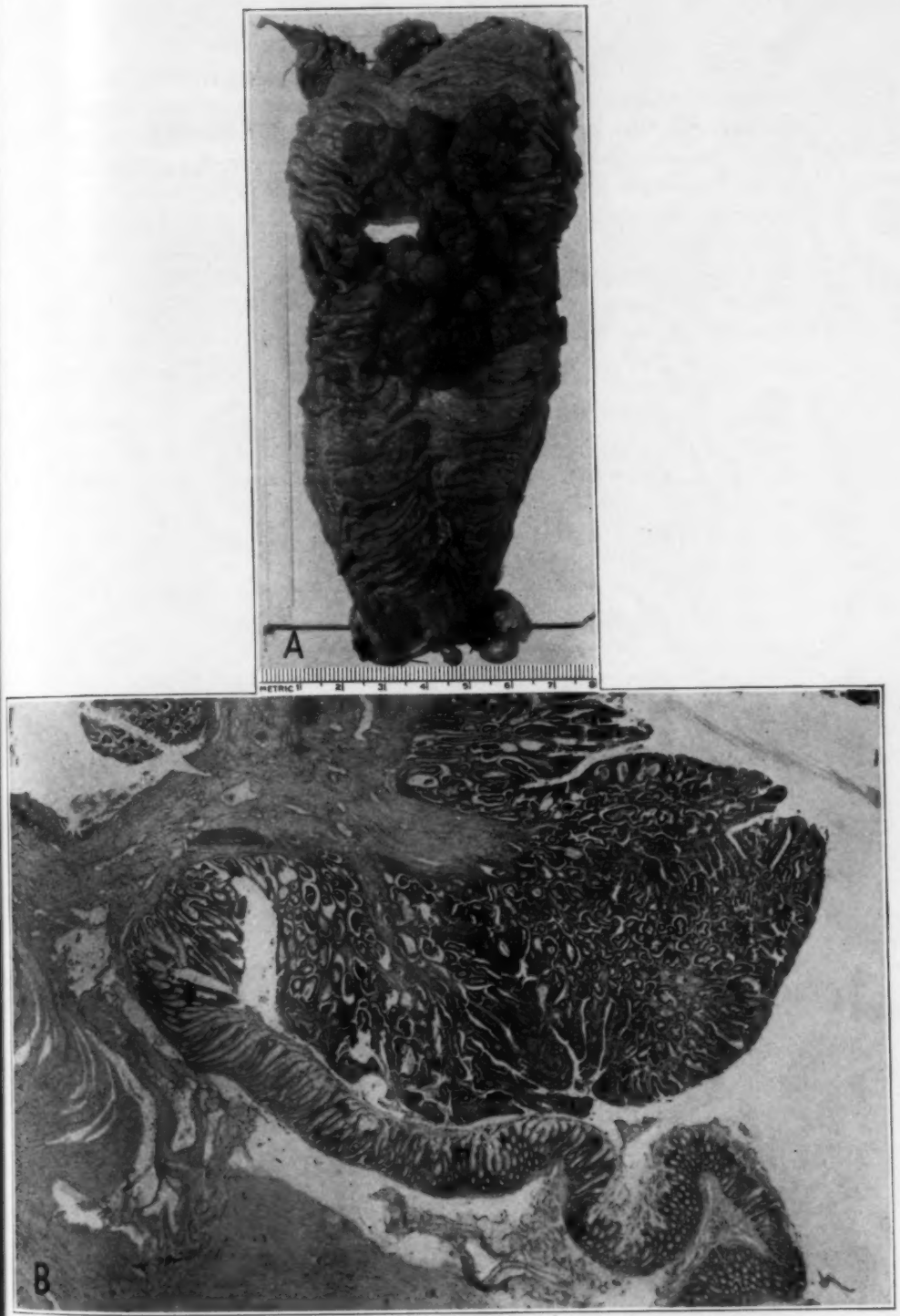

Fig. 8.—*A*, papilloma of the descending colon producing obstruction. *B*, photomicrograph of a portion of the papilloma compared to the normal mucosa of the bowel adjacent to it.

these tumors in my early management of them were subjected to repeated fulguration, which is usually inadequate for the larger growths. In none of the repeatedly irritated tumors did malignancy supervene. If removal of these tumors is incomplete, recurrence will promptly supervene, but in my experience the recurrences have been benign histologically. When malignant changes occur in this type of growth they usually occur in the center of the papilloma. Of all the benign polypoid growths occurring in the large bowel, the papilloma most nearly resembles in gross appearance a carcinoma, and, conversely, many carcinomas take on a distinctly papillomatous appearance. In histologic examination of this type of growth it is therefore of particular importance that the whole tumor be examined, as the base and center of the mass are most likely to show carcinomatous changes. Of great importance in determination of the kind of operation (local or radical) to perform are the gross appearance and feel of the tumor, any evidence of induration or ulceration giving clear indication for radical removal of the segment of bowel containing the tumor.

One of the most striking and convincing arguments in favor of the relation of polyps of the large bowel to the development of carcinoma is seen in multiple polyposis. In the presence of this lesion the entire colon and rectum may be studded with polyps, thousands of them, varying in size from a millimeter to several centimeters, with either sessile or pedunculated attachments and with the histologic framework of an adenoma, a papilloma or a mixture of the two (fig. 9). In many of the polyps the regular structure in relation to the connective tissue stalk is lost, and the branching tubules with heavily staining multiple-layered cells indicate a tendency to uncontrolled growth. Clinically considered, the only etiologic basis of this bizarre and unusual tendency to tumor formation is a hereditary one, there being a remarkable occurrence of this lesion in successive generations of a family. The other definite and alarming tendency of these polyps is to malignant degeneration, there being not infrequently three to four areas in the colon where carcinoma has developed. In Loring's case (fig. 9*A*) 3 definite carcinomas were found in the colon. This decided tendency to carcinomatous degeneration in multiple polyposis has led nearly all surgeons to advise graded removal of the entire large bowel before carcinoma develops.

Akin to this lesion but lacking the hereditary factor and the extensive involvement of the colon is the occurrence of multiple polyps in the large bowel, where 3 to 10 may be present. These are often of varying sizes and may be widely separated. It seems probable that the malignant degeneration of these polyps is responsible for the increasing recognition of multiple cancers of the large bowel. I have observed 5 examples

of double cancer of the large bowel, in 4 of which the condition was highly suggestive of carcinomatous degeneration of polyps. A short history of a case of this kind will be given.

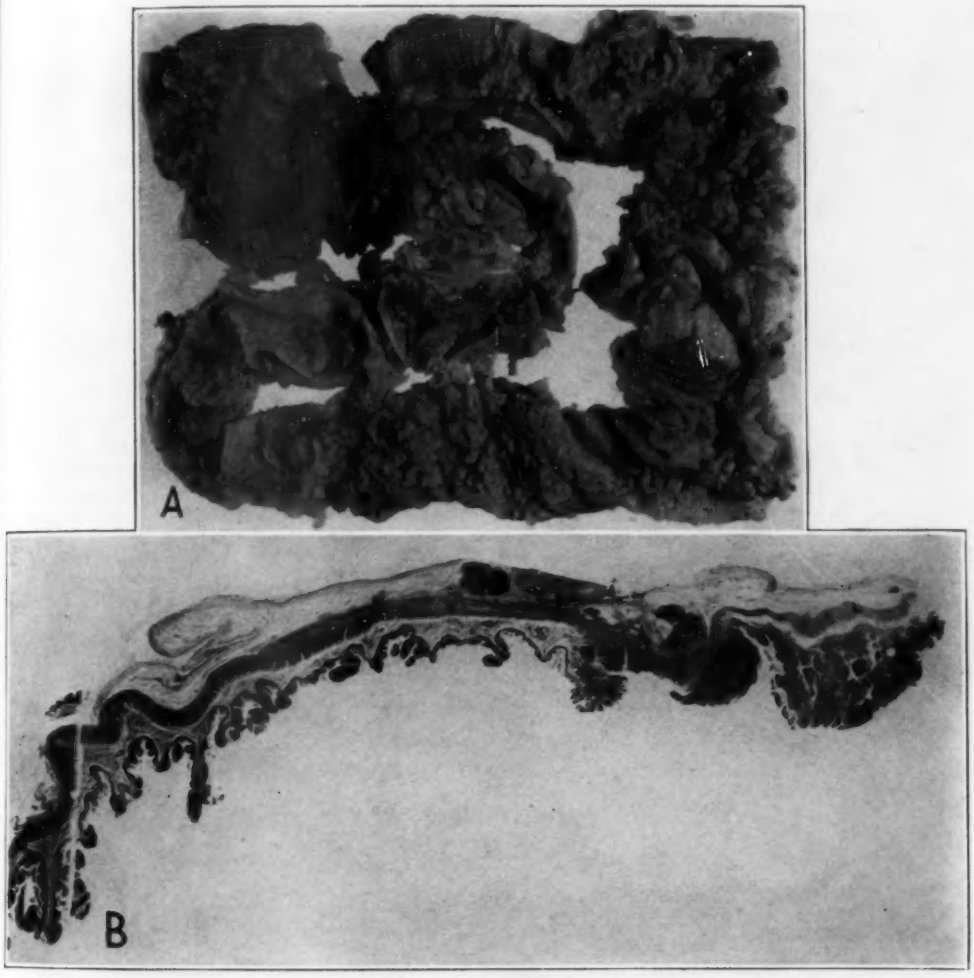

Fig. 9.—*A*, postmortem specimen of multiple polyposis of the colon which included three separate carcinomas with regional metastases. *B*, giant section of the colon shown in *A* (Dr. Mark Loring), showing the various polypoid structures.

A fat man 52 years of age had a definite carcinoma of the ampulla of the rectum in the form of a polypoid mass protruding into the lumen of the bowel, which was ulcerated and indurated and from which a biopsy specimen was taken, showing definite invasion of cancer cells (fig. 10). About 3 inches (7.6 cm.) above this lesion was a flat, sessile attached polyp which was not ulcerated and

had every appearance of being benign. No other lesions were suspected, and a fluoroscopic study of the colon revealed no other lesions. A one stage abdominoperineal resection of the rectum was carried out, with some difficulty due to the adiposity. The patient died of peritonitis. The autopsy revealed 2 other polyps of the transverse colon, one about 2 cm. in diameter, with definite carcinomatous degeneration (fig. 11).

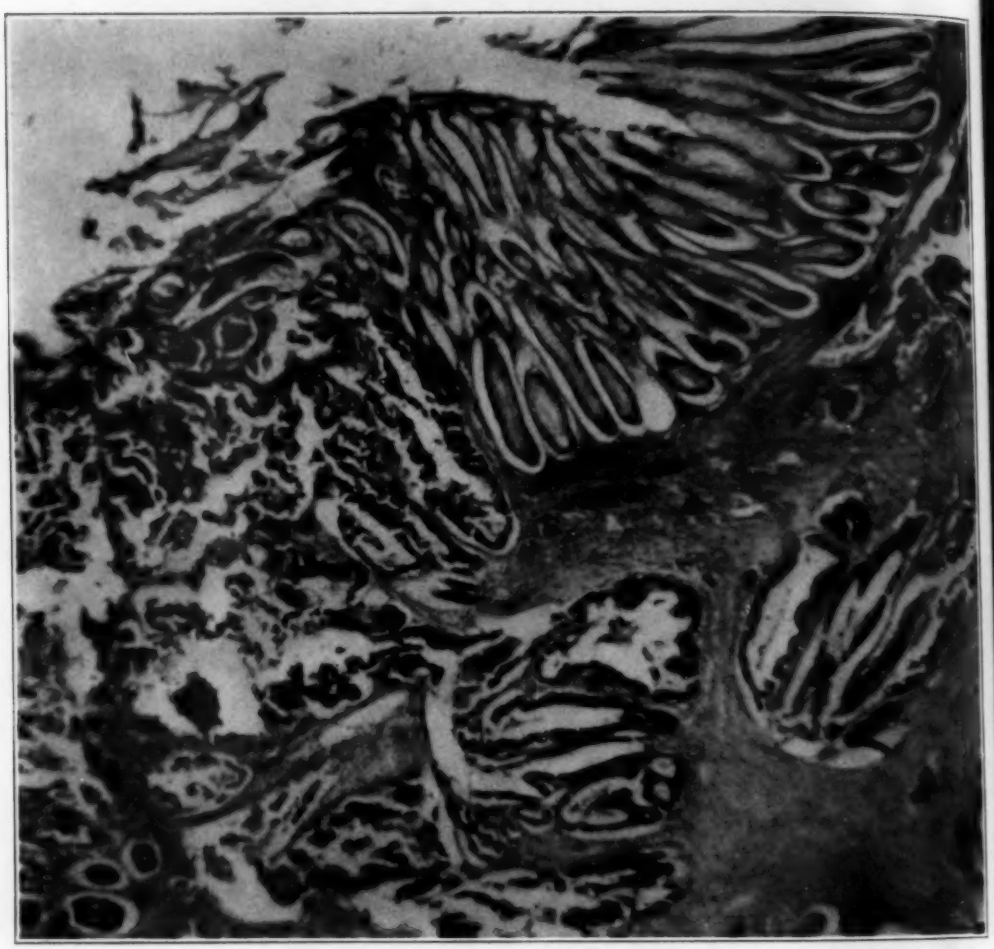

Fig. 10.—*A*, carcinoma of the rectum with a malignant polyp of the transverse colon (fig. 11).

Dr. W. B. Gabriel, of St. Mark's Hospital, London, England, has several interesting specimens illustrating these same points.

Of very much less importance or of no importance in their carcinomatous tendency are the so-called lymphoid polyps, which may appear as

multiple slightly elevated flat lesions a few millimeters in diameter, affecting the colon and rectum, and which are really a form of lymphoid hyperplasia (fig. 12 *A*).

Of more clinical interest but lacking carcinomatous tendencies are the large lymph polyps, of which I have seen 5 instances in the rectum.

Fig. 11.—Malignant polyp of the transverse colon associated with carcinoma of the rectum. Note the invasion of the tumor through the muscularis mucosa at *A*.

In the first 2 cases there was a single polyp in the rectum, about 2 cm. in diameter, with sessile attachment. The tumor was rather hard. In appearance the mucosa over the polyp was normal, and it appeared as if a globular mass were situated in the bowel, immediately beneath the

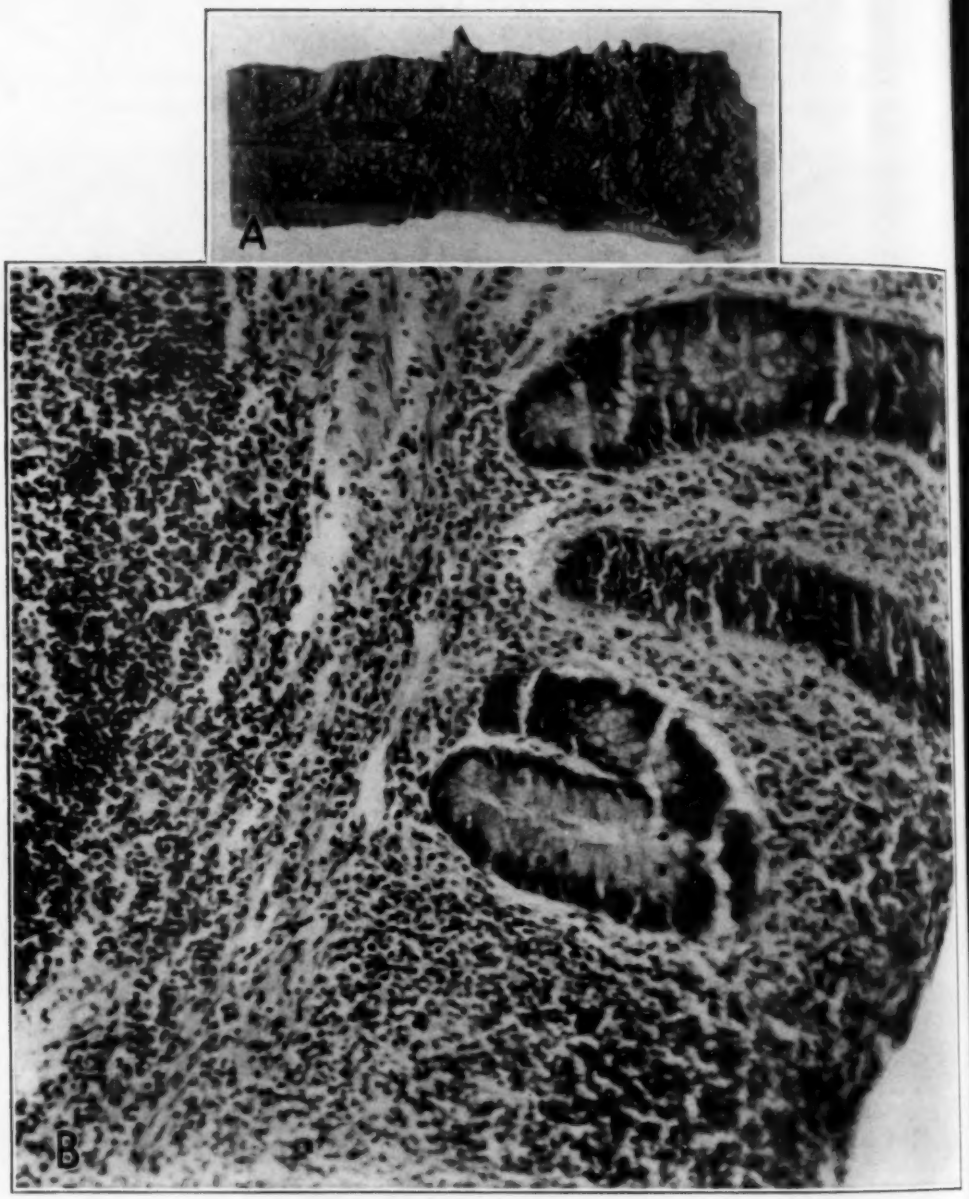

Fig. 12.—*A*, multiple lymphoid polyps of the colon, from Westhues' monograph.[2] *B*, large lymphoid polyp of the rectum with epithelial tubules separated by lymphocytic infiltration.

mucosa. On removal of the mass the feeling was substantiated; on microscopic examination the mucosa was normal, but beneath it was a large accumulation of lymphoid tissue (fig. 12*B*). This may have been a simple inflammatory hyperplasia of the normal lymphoid tissue.

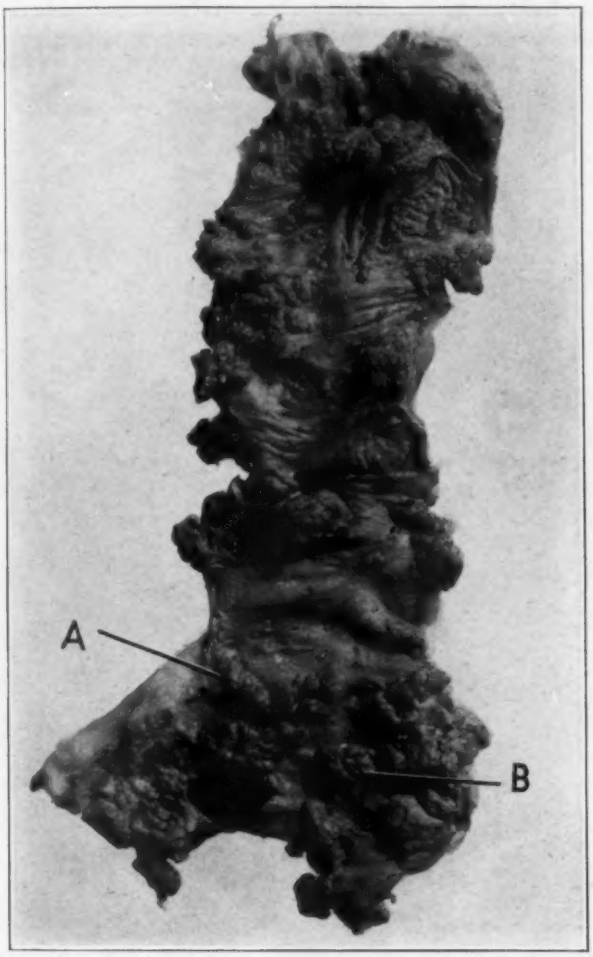

Fig. 13.—Multiple inflammatory polyps of various types found in a colon which was the seat of amebic ulceration.

A third case was more confusing. A woman 50 years of age was referred to me with the probable diagnosis of carcinoma of the rectum. On examination a mass about 4 cm. in diameter, consisting of 2 definite polypoid masses, was present on the anterior wall of the rectum, about 3 inches (7.6 cm.) from the anus. The patient had been bleeding, and

through the proctoscope it was seen that the base of the polypoid mass was ulcerated, though the major portion of the mass was covered with smooth epithelium. A biopsy specimen taken through the ulcerated area revealed evidence of a lymphoid polyp covered with epithelium, without adenomatous or papillomatous degeneration. Complete removal of the mass showed a typical lymphoid polyp. Whether the ulceration of the lesion had any potentialities as far as carcinoma is concerned is hard to say.

Fig. 14.—Section through *A* in figure 13, which shows hyperplasia of the epithelial elements of the mucosa as well as an inflammatory process in the otherwise normal mucosa.

The last classification of polyps involving the large bowel is the inflammatory type, to which some reference has been made. The most striking examples of inflammatory polyps are those seen following extensive destruction of the mucosa of the bowel as a result of amebic dysentery or ulcerative colitis (figs. 13, 14 and 15). The polyps result from an inflammatory hyperplasia of persistent small islands of mucosa between

areas of ulceration. One patient had such a polyp as large as a goose egg in the rectum, which he would not allow to be removed.

One of the most interesting examples of this type of polyp was seen in a man 38 years of age. The level of hemoglobin had dropped to 28 per cent owing to repeated bleeding from the rectum. By proctoscopic examination, at 12 cm. from the anus an inflamed area with numerous finely lobulated papillomatous tumors was seen. Unfortunately no biopsy was done. A colostomy was performed, and on repeated proctoscopic examination a gradual recession of the papillary tumors

Fig. 15.—Section through *B* in figure 13, showing a polypoid tumor with a connective tissue stalk and branching epithelial tubules with heavily staining nuclei. This polyp developed in the presence and probably as the result of chronic inflammation of the intestinal mucosa from amebic dysentery. Its appearance cannot be distinguished from that of the adenomatous polyps which are called true tumors.

took place until, at the end of ten months, no tumor was visible, and the bowel appeared practically normal. About nine months after colostomy several elevated polypoid masses, each about 0.5 cm. in diameter, appeared on the exposed mucosa of the colostomy stoma. One was excised, and a section was made. This cor-

responded to the inflammatory hyperplasia already described. At the request of the patient the colostomy stoma was closed. Bleeding again appeared, and the rectum showed marked inflammation without tumor formation. The rectum was removed. No evidence of tumor growth was found. This patient well exemplifies the influence of inflammation on hyperplasia of the mucosa of the colon, which closely resembles tumor formation.

One of the most interesting examples of the influence of inflammation on changes in the epithelium of the large bowel was readily seen at postmortem examination of a woman who had suffered with amebic dysentery for three years. The bowel showed many discrete ulcers from which amebas were isolated. The sigmoid flexure of the colon and the rectum particularly were the sites of numerous polypoid changes, ranging from small millimeter elevations to well developed flat and pedunculated tumors. Histologic examination of the bowel showed widespread inflammation of the mucosa with desquamation or necrosis of the surface cells. The elevations and tumor-like growths on the mucosa ranged from simple hyperplasia in which reduplications of the elements of the mucosa without increased staining of the cells were seen to typical adenoma formation with a connective tissue stalk and branching tubules with heavily staining nuclei. The sections referred to are shown in figures 14 and 15. In this case the whole problem of the relation of inflammation to tumor formation is brought acutely into focus.

One other example of this relation must be mentioned. A young woman in her late twenties had suffered from extensive ulcerative colitis for several years. Proctoscopic examination by her physician in Ann Arbor, Mich., because of first bleeding revealed a small papillary tumor at the rectosigmoid juncture. This was completely removed through the proctoscope and after examination by the late Dr. A. Warthin was pronounced carcinoma. Shortly afterward I examined the patient proctoscopically but could find no lesion except extensive ulcerative colitis. Within two months another examination revealed a small carcinoma at the rectosigmoid juncture. It is, of course, impossible to prove that the original tumor was an inflammatory polyp which had undergone malignant degeneration, but the whole course of events is of more than ordinary interest.

The various types of polypoid growths occurring in the large bowel having been reviewed and their inclination to carcinoma formation having been indicated in a general way, the results of Feyrter's study of 1,100 colons containing 1,017 polyps may be interesting. He found no case of multiple polyposis and none of papilloma. There were 15 patients in whom carcinoma of the colon was the cause of death and 4 in whom latent carcinoma was present. In 350 patients with

polyps of the colon, 6 of the polyps were carcinomatous histologically and 4 were suggestive of carcinoma. Of 1,017 polyps of the colon from 1,800 autopsies:

	Per Cent
762 were millet seed size	75
175 were pea size	17
35 were cherry stone size	3.5
22 were hazelnut size	2.2
5 were cherry size	0.5
4 were almond size	0.4
8 were bean size	0.8
7 were larger	0.7

If adenomas alone are considered:

Age, Years	Males	Females
0 to 14 in 100 cases	No polyps	No polyps
15 to 34 in 100 cases	No polyps	1 polyp
35 to 44 in 100 cases	2 polyps	4 polyps
45 to 54 in 1/8 of the cases	polyps	1/10 had polyps
55 to 64 in 1/4 of the cases	polyps	1/10 had polyps
65 to 74 in 1/3 of the cases	polyps	1/8 had polyps
75 to 87 in 1/3 of the cases	polyps	1/3 had polyps

If age (in years) is considered for all of the lesions found:

Age, Years

0 to 14: Of 100 patients, 2 had polyps
15 to 34: Of 100 patients, 5 had polyps
35 to 44: 1/6 of the patients had polyps
45 to 54: 1/3 of the patients had polyps
55 to 64: 1/2 of the patients had polyps
65 to 74: 2/3 of the patients had polyps
75 to 87: 3/4 of the patients had polyps

As a result of this thoroughgoing study, Feyrter has called attention to the polypoid lesions in which little histologic evidence of change from normal epithelium is present and also to polyps in which more or less lack of differentiation of epithelium, lack of order of the epithelial elements, differences in the depth of cell layers and marked differences of staining qualities of the cells and nuclei exist. He has stated that one must differentiate between hyperplasia that remains such, hyperplasia that develops into an adenoma and hyperplasia that develops into a cancer. He holds with Oberdorpher and Lubarsch that infiltrating destructive growth is the principal sign of cancer. The other signs of increased activity of epithelial growth are suggestive but offer no proof.

Westhues [2] has studied 100 cases of rectal carcinoma with accompanying polyps and an unstated number of polyps of the rectum and

colon occurring because of symptoms caused by the polyps. He has particularly concerned himself with the flat-based adenomas of pea size and larger, found near carcinomas of the large bowel and exhibiting the gross change in color and the lack of differentiation of the epithelium, evidence of disorganized growth microscopically. He differs from many who have interested themselves in this subject by suggesting that carcinoma is actually present in these polyps before evidence of destructive invasion takes place.

It is interesting to speculate as to the time carcinoma actually starts and to recognize the atypical changes occurring in the epithelium of these polyps before actual invasion takes place. The pathologist may have his "hunch," or "feel," about the matter, but to describe definite morphologic characteristics of a carcinoma cell which has not invaded the basement membrane is difficult. Boist at the International Cancer Congress in 1933 remarked that there are no specific morphologic changes on which under all conditions a cancer cell can be diagnosed with surety. He added, however, that the changes observed in the nucleus and protoplasm in many malignant growths are so striking that apart from specificity they can lead to no other interpretation. Kaufman and Maresch pertinently observed that in this problem there may be not only polyps with a carcinomatous tendency but that there are also polyps which are malignant from the first.

Westhues has placed great importance on the frequent presence of polyps in the colon and rectum accompanying a carcinoma. In his 100 cases of rectal carcinoma he found some type of polypoid change in the mucosa of the large bowel in 45 per cent, and he stated the opinion that at least 15 per cent of these carcinomas arose from polyps. In my own material the presence of millet seed–sized elevations around the carcinoma was common, occurring in 40 of 128 specimens of carcinoma of the rectum and colon which were carefully examined, but the occurrence of larger polyps accompanying carcinoma of the large bowel was 13 per cent, polyps occurring in 17 of 128 specimens examined.

Excluding the millet seed–sized polyp seen around carcinomas of the rectum, I have examined and in the great majority removed polyps from the rectum and colon of 101 patients. The results of my study of this material convinced me that there was a gradual transition of these polypoid growths from hyperplasia to adenoma formation, showing a simple differentiated epithelial structure and then proceeding to a less ordered and less differentiated epithelial growth and finally to actual carcinomatous invasion. The most convincing evidence of the malignant tendency of these polyps is the actual carcinomatous change in a lesion the major part of which is benign from both a gross and a histologic viewpoint. I have not included in my classification the

1 to 2 mm. hyperplasias which are rather commonly seen in the colon and rectum around carcinomas or developing on the exposed mucosa of a colostomy.

I. Adenomas		
Children	5	
Adults—		
Rectum	31	
Colon	11	
		47
(17 associated with cancer)		
II. Papillomas		
Rectum	23	
Colon	4	
		27
Multiple polyposis—colon		2
1 with 3 malignancies		
Small intestines and colon	1	
Small and large bowel	1	
Multiple polyps		5
III. Lymphoid polyps		5
IV. Inflammatory polyps		6
V. Polyps with early malignancy		9
		101

The hyperplasias are probably inflammatory in origin, as they appear on the exposed mucosa of colostomy openings, near ulcerating carcinomas and on the intestinal mucosa of old persons and histologically have a marked leukocytic infiltration in the submucosa. As a rule the color and staining qualities of the epithelium are normal, but occasionally the lesion is darker than the surrounding mucosa, and the tubules are branching. In other words, there is a move toward tumor formation.

More than half of the adenomas examined in my series were of simple structure. The epithelium was regular, with evenly staining nuclei with few mitoses. A few of the adenomas had a mixed inflammatory and myxoid stroma containing small acinar cysts. This is a common structure in the adenomas of childhood. In contrast to this picture were other adenomas, in which were observed branching tubules, increased cell layers, increased staining of the protoplasm and nuclei, frequent mitotic figures, less differentiation of the epithelium in general and some loss of relation between the epithelium and the muscularis

mucosa. These changes are mostly seen on the periphery of the adenoma. In no area could invasion be said to have taken place, but if certain fields in these polyps are compared to fields in a proved carcinoma it would be difficult to distinguish between them (fig. 16). This emphasizes anew the importance of having the whole tumor to examine and of ascertaining the appearance and consistency of the polyps so that areas of ulceration or induration can be determined.

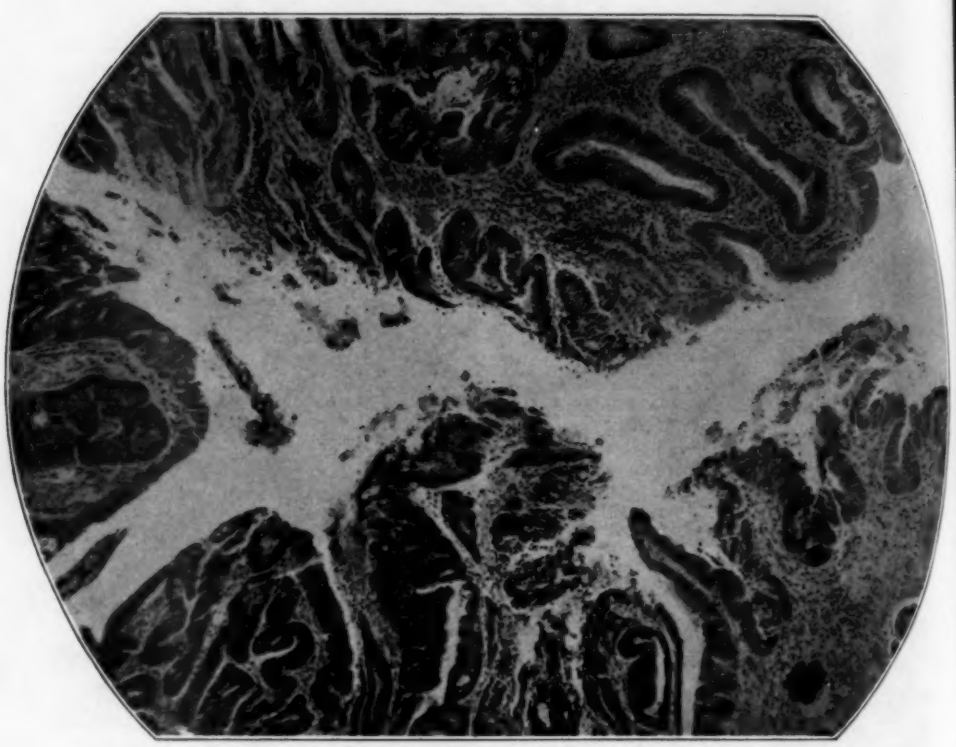

Fig. 16.—Bizarre epithelial arrangement with little differentiation, resembling carcinoma, in a polyp of the rectum which was neither indurated nor ulcerated. Local removal of the polyp resulted in cure.

There were 3 small adenomas (1 to 2 cm. in diameter) undergoing early malignant changes. This was suspected by slight ulceration of the lesion. In 2 of these the carcinomatous ulcer was not more than 2 mm. in diameter, and in the third the pedunculated adenoma was superficially ulcerated (figs. 17, 18 and 19). These constitute the earliest evidence of malignancy in the rectum which I have seen.

There were 4 large flat adenomas, 8 to 6 cm. in diameter, in which malignancy was suspected but very difficult to prove until after radical

removal of the tumor and surrounding bowel. Three of these were in the sigmoid flexure of the colon and 1 in the rectum. The flat soft tumor in the ampulla of the rectum was in a perfectly healthy man whose only symptom had been bleeding. The biopsy was inconclusive, but because of one small area of induration a radical removal of the section

Fig. 17.—Drawing of a resected rectum containing a small carcinomatous ulcer on an adenoma, a flat adenoma and a small nodule of hyperplasia, the latter shown in figure 1.

was carried out. The pictures of the gross lesion, the results of biopsy and the sections taken through the area of induration accompany the text and bear out the wisdom of radical removal of polypoid tumors of the bowel when only a suspicion of their malignancy exists because of induration in a part of the tumor (figs. 20, 21 and 22).

In the group of 27 flat-based papillomas or villous tumors occurring for the most part in the rectum, their histologic character and structure is in general more complicated than in adenomas of the bowel. The long, many-branching tubules, with many-layered cells, increased staining properties and nuclear mitoses, indicate active growth. Grossly

Fig. 18.—Junction of the adenoma and the carcinomatous ulcer shown in figure 17.

these tumors become large, some being as large as the adult fist and obstructing the bowel. They may remain in the bowel for years without undergoing malignant change, although grossly they have a striking resemblance to carcinoma. When malignant changes occur in these

tumors, the depth and not the periphery of the tumor is apt to be involved, and an area of induration develops (fig. 23). Biopsy of a specimen of the papilloma surrounding this area may show perfectly benign noninvading papilloma, but biopsy of a specimen taken through the area of induration reveals infiltrating carcinoma. Papillomas, because

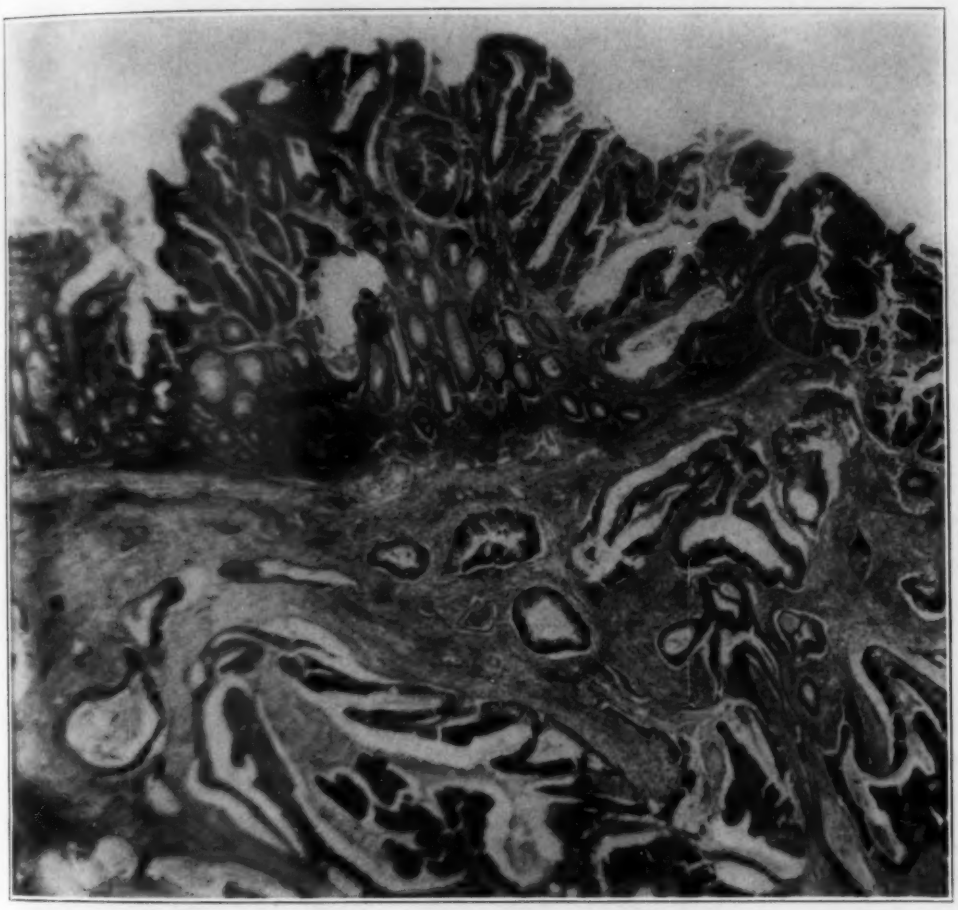

Fig. 19.—Two millimeter carcinomatous ulcer on a pedunculated adenoma.

of the evidence of epithelial growth changes, as deeply staining many-layered cells, mitoses and branching tubules, are often called carcinoma grade I. This, to my mind, is an error, for ulceration and invasion are the only certain criteria of malignancy. It should in fairness be stated that in about half of my specimens some loss of differentiation of the tubular epithelium was present and that there was less regular

relation of the epithelium to the connective tissue stalk and the muscularis mucosa than is normal. In view of the fact that these tumors are undoubtedly premalignant, they must be thoroughly removed, but local removal is indicated whenever possible if no induration or ulcera-

Fig. 20.—Soft, large, flat tumor of the rectum. This type of growth is hard to diagnose as to malignancy or benignity.

tion of the tumor is present. It is pertinent to say that among these 27 cases no malignancy has occurred after local removal of the tumor. In 3 cases local recurrence of the papilloma took place, but after removal of the recurrent growth the patients have been well for periods varying from two to six years.

In my table, group V is listed as polyps with early malignancy. Three of these were concerned with papillomatous soft growths in the rectum, where slight induration was present. Biopsy of material from these areas showed invading carcinoma, and radical operations were carried out.

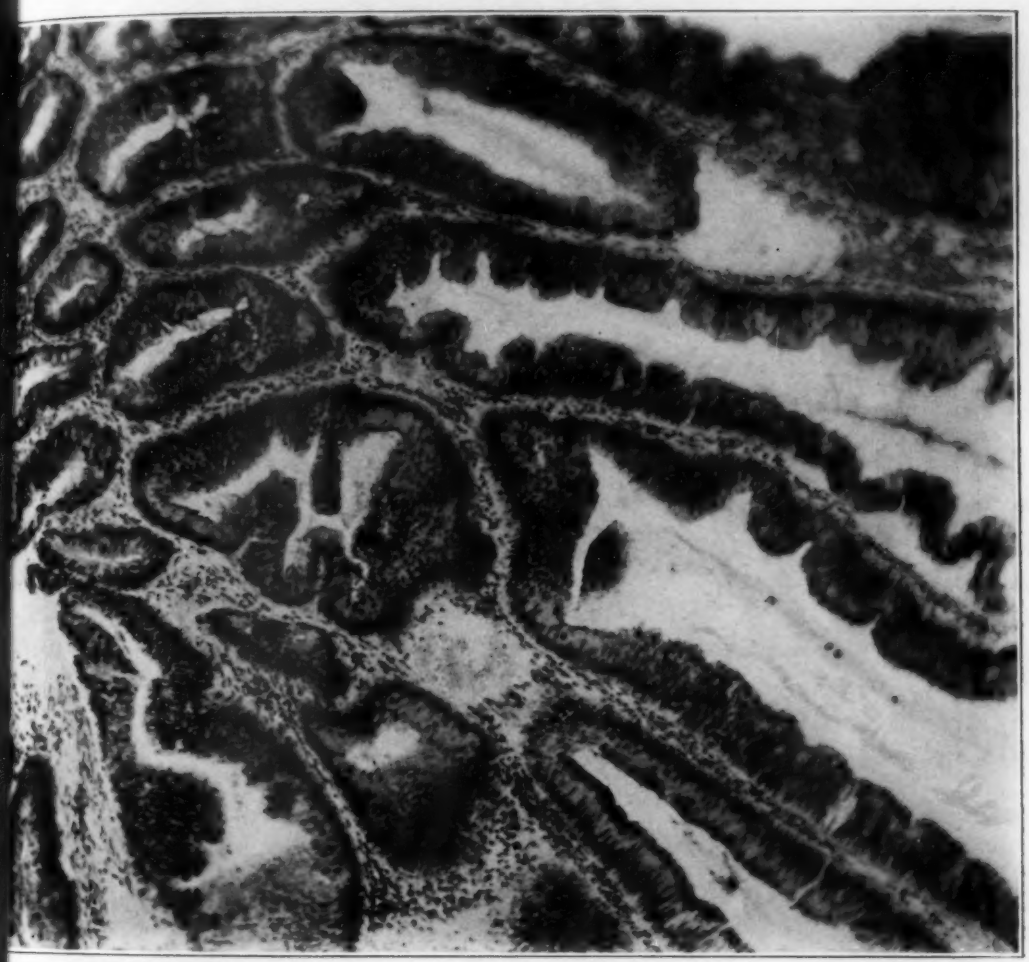

Fig. 21.—Biopsy of the surface of the tumor in figure 20 was suggestive of carcinoma, but the diagnosis was not certain.

SUMMARY AND CONCLUSIONS

It can be fairly said that in the mucosa of the large bowel there is a gross and gradual histologic transition from hyperplasia to adenoma or papilloma to carcinoma. Whether the inherent tendency to carcinoma in any one of these lesions is present from the start is not known.

Carcinomatous changes in these lesions can be safely diagnosed only by gross evidence of induration or ulceration and by histologic evidence of invasion, in which instance tumor cells are found breaking through the muscularis mucosa.

Fig. 22.—After radical removal of the tumor in figure 20, sections taken through the base of the tumor showed typical carcinomatous infiltration.

While many of the polyps of the colon remain benign for years, they cannot be trusted to do so and should be thoroughly removed, locally if benign and radically if evidence of malignancy exists.

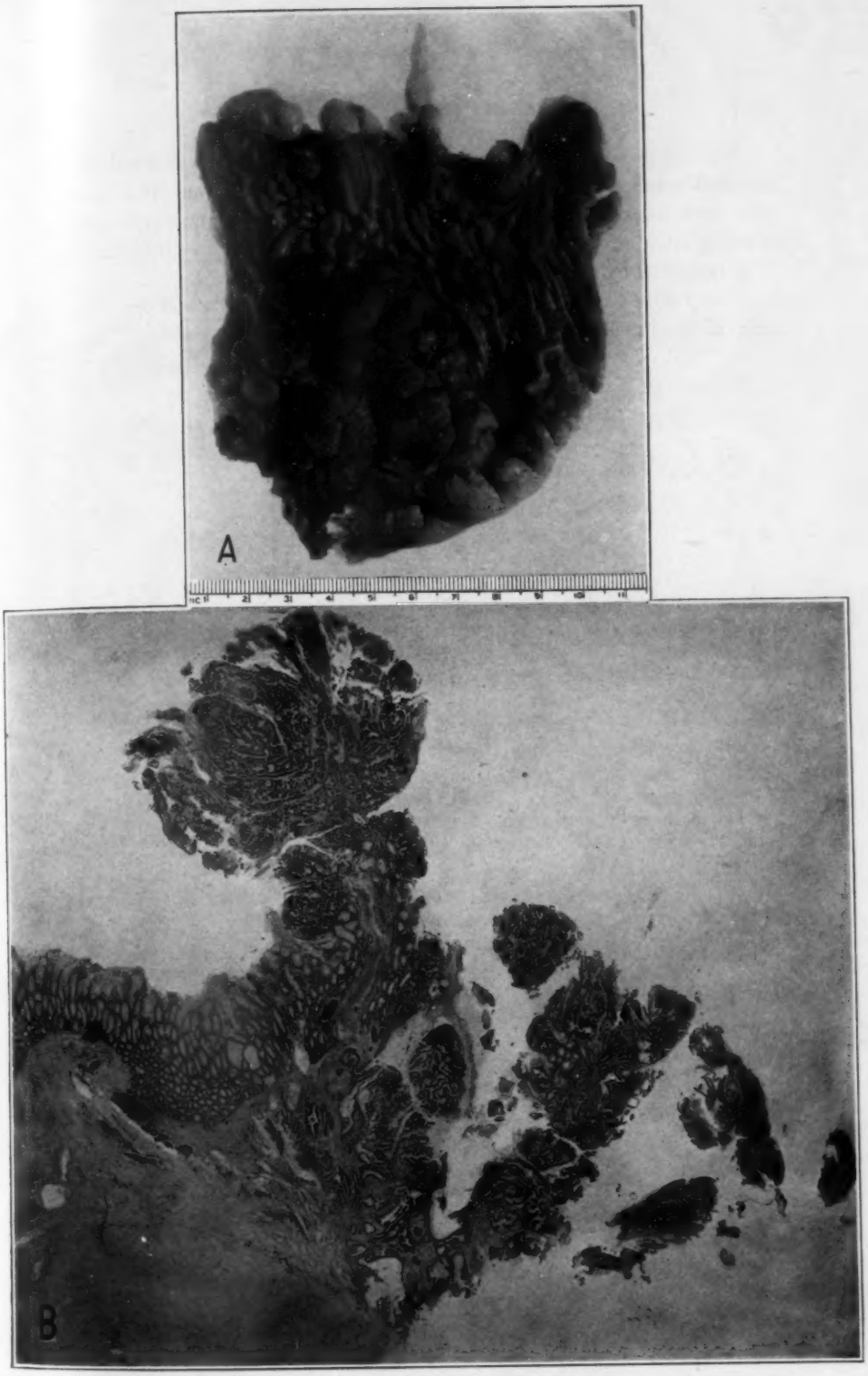

Fig. 23.—*A*, diffuse adenomatous tumor of the rectosigmoid juncture in a 23 year old woman. Its malignancy was questionable. *B*, photomicrograph of the tumor, showing definite carcinomatous infiltration.

The results of biopsy may not be conclusive for diagnosis unless the material is taken from an area of ulceration or induration. It is impossible with many of these lesions for a pathologist to make a diagnosis of malignancy or benignity from a small piece of tissue taken at random. It is better to examine the whole tumor.

The earliest carcinomas I have seen in the large bowel are 1 to 2 mm. ulcerating lesions found on polyps.

BARBERRY

ANCIENT REMEDY; NEW GERMICIDE

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Some time ago Mr. William H. Wood, of Brownsville, Texas, called my attention to infusion of algerita root, a remedy used by the Indians of Texas and Mexico for many ailments.

As many of these ailments were infectious processes, the following experiment was carried out in order to learn whether the infusion possessed any antiseptic or germicidal properties.

METHOD

Five hundred grams of crushed algerita root was boiled for thirty minutes in 2 liters of distilled water and the liquid filtered through gauze. This infusion was sterilized in the autoclave and used as follows: One-tenth cubic centimeter of a twenty-four hour broth culture of scarlet fever streptococcus was added to each of six test tubes, each containing 10 cc. of ordinary nutrient broth with 0.1 cc. of sterile blood added. To one of these tubes 0.1 cc. of algerita root infusion was added; to four tubes, 0.2 cc., 0.5 cc., 1.0 cc. and 3.0 cc., respectively, was added, and to the remaining tube no infusion was added. The six tubes were incubated for twenty-four hours; then 0.1 cc. of the well mixed contents of each tube was added to 10 cc. of broth, and 0.1 cc. of this broth was added to 10 cc. of melted nutrient agar at 40 C. with 0.5 cc. of blood added. Blood agar plates were poured and incubated for twenty-four hours.

The Petri plate of the control tube, with no infusion added, contained innumerable colonies of streptococci at the end of the incubation period. The Petri plate of the culture tube containing 0.1 cc. of infusion showed a few colonies of streptococci, and the remaining plates contained no growth.

It will be noted that in plating out the mixture of infusion being tested, bacterial suspension and broth, a dilution of 1:100 was made, which did away with any inhibitory action of small amounts of infusion carried over into the agar plates.

The experiment indicated, therefore, that the algerita root infusion was germicidal in the tubes containing 0.2 cc. or more. Repetition of this experiment gave consistent results.

In order to find out the length of time required to kill streptococci, 0.5 cc. of a twenty-four hour broth culture of erysipelas streptococcus was added to 10 cc. of nutrient broth containing 0.5 cc. of algerita infusion. The mixture was incubated; after thirty minutes 0.1 cc. of the mixture was added to 10 cc. of broth, and

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0.1 cc. of this mixture was plated out. In a similar way, 0.1 cc. of the mixture was plated out after one, two, four, seven, sixteen and twenty-four hours. All the plates up to those made after seven hours contained many colonies, when only 115 colonies were found; in sixteen hours 10 colonies were found, and in twenty-four hours no growth was present.

In the dilution used, (1:20), then, the streptococci were killed only after seven to twenty-four hours of contact.

With various dilutions of mercury bichloride used in the same way as the infusion was used in the second experiment, 0.5 cc. of a 1:10,000 solution of mercury bichloride added to 0.1 cc. of twenty-four hour culture of erysipelas streptococcus in 10 cc. of broth took eight hours to kill, so that the infusion has about the same germicidal power as a 1:10,000 solution of mercury bichloride.

Experiments were carried out to compare the action of algerita infusion on different bacteria. These tests were done just as was done with scarlet fever streptococci except for the variety of organisms used. The result is shown in the accompanying table.

Effect of Infusion on Different Bacteria

Organism	Number of Colonies Growing on Plates After 24 to 48 Hours with Different Quantities of Infusion						
	Broth and Bacteria Alone	0.1 Cc.	0.2 Cc.	0.5 Cc.	1 Cc.	2 Cc.	3 Cc.
Hemolytic streptococcus of tonsillitis	Innumerable	Many	0	0	0	0	0
Scarlet fever streptococcus	Innumerable	10	0	0	0	0	0
Pneumococcus type I	Innumerable	Many	Many	70	0	0	0
Staphylococcus	Innumerable	Innumerable	Innumerable	150	15	0	0
Streptococcus viridans	Innumerable	Many	Many	Many	0	0	0
Typhoid bacillus	Innumerable	All plates contained as many colonies as control					
Diphtheria bacillus	Innumerable	0	0	0	0	0	0
Brucella melitensis	Innumerable	Many	Many	Many	3	0	0
Erysipelas streptococcus	Innumerable	Many	50	0	0	0	0
Brucella abortus	Innumerable	Many	Many	6	0	0	0

It will be noted at once that there is a very interesting selective action, for in the tubes containing 0.2 cc. of infusion, hemolytic streptococci and diphtheria bacilli were killed, whereas staphylococci and pneumococci required about five times as much infusion. The brucella organisms were between the other two groups, while typhoid bacilli grew as well in all concentrations used as in nutrient broth alone. It was also observed that the infusion had to be kept under sterile precautions or preservatives added to prevent the growth of molds.

In view of the remarkable selective germicidal action of the infusion, it seemed worth while to investigate its toxicity for animals.

A rabbit weighing 2,075 Gm. was given 0.3 cc. of filtered sterile infusion intravenously on April 4, 1939. Three days later the same animal was given 4 cc. Some convulsive movements were noted, but the animal remained well until

December 26 (about seven months later), when it weighed 2,879 Gm. and had normal urine. Between Jan. 1 and March 4, 1940, 1 cc. was given intravenously three or four days a week; in all, 21 cc. On April 25 the rabbit seemed well, weighed 2,841 Gm. and had normal urine.

Two rabbits were given 20 cc. of infusion by stomach tube daily for two weeks and remained apparently well until observation ceased, four months later. On the other hand, 2 rabbits receiving 5 cc. intravenously died at once.

Amounts up to 0.2 cc. may be given to mice subcutaneously without effect, but 0.3 cc. occasionally proves fatal, and 0.5 cc. or more kills regularly.

COMMENT

These experiments, together with reports that the Indians and old settlers in Texas take by mouth amounts of the infusion up to several ounces three times a day, show that algerita root infusion has considerable germicidal power, with a relatively low toxicity.

On looking up the botanic classification of the algerita bush, it was found to belong to the large barberry family of shrubs, which has an extremely wide distribution in the world. Algerita is also known as Berberis trifoliatis, Mahonia trifoliata and Odosteman trifoliatis.

Hart [1] stated that algerita root has long been used by old settlers and Indians in Mexico and Texas for sore eyes, sore mouth, cutaneous diseases and gonorrhea. He analyzed the root and found that it contained 1.49 per cent of berberine ($C_{20}H_{19}NO_5$), a yellow dye characteristic of the barberry family. Unlike Berberis vulgaris, however, it contained no hydrastine.

Chopra [2] listed several varieties of barberry, including Berberis lycium and Berberis aristata, used in India by the natives for various ailments, including malaria, syphilis, oriental boil and duodenal ulcer.

According to Culbreth,[3] Berberis canadensis was official from 1860 to 1880 and was used for dysentery, dropsy and many other diseases. Other plants containing berberine, such as calumba and goldenseal, are used in Africa, Madagascar and other parts of the world for malaria and various fevers.

Cushny [4] stated that the main pharmacologic action of the drugs containing berberine is that of a bitter tonic and that berberine, aside from its bitter taste, has no pharmacologic action.

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1. Hart, M. C.: Am. J. Pharm. **88**:301, 1916.

2. Chopra, R. N.: Indigenous Plants of India: Their Medical and Economic Aspects, Calcutta, Art Press, 1933.

3. Culbreth, D. M. R.: A Manual of Materia Medica and Pharmacology, ed. 4. Philadelphia, Lea Brothers & Co., 1906.

4. Cushny, A. R.: Textbook of Pharmacology and Therapeutics, ed. 9, Philadelphia, Lea & Febiger, 1928.

Flückiger and Hanbury [5] stated that Berberis lycium was used by the ancient Greek and Roman physicians, and it is mentioned by Diodoscorides, Pliny and Celsus. It was particularly valued for sore eyes and catarrhal diseases.

The only instance of an adequate investigation of germicidal properties of berberis on its products is to be found in a report by Das Gupta [6] and another by Warma [7] on the use of 3 cc. of a 2 per cent solution of berberine acid sulfate injected into the lesions of oriental boil. According to Das Gupta, the injections are followed by rapid disappearance in biopsy specimens of the Leishman-Donovan bodies and rapid clinical improvement. Others have confirmed these observations. That the germicidal properties of algerita root infusion are probably due to its berberine content is shown by substituting a 0.1 per cent solution of berberine sulfate Merck for the algerita infusion as described. It was found that from 0.05 cc. to 0.1 cc. of the 1 per cent berberine solution in 10 cc. of broth with 0.1 cc. of erysipelas streptococcus twenty-four hour broth culture regularly killed the bacteria, whereas it took about 0.2 cc. of the infusion to kill the same organism. The berberine content of the infusion is about ¼ of 1 per cent, so that it is unnecessary to assume any other germicidal substance in the infusion other than berberine.

It was also found that the time required for a 1 per cent solution of berberine to kill erysipelas streptococci was about eight hours in the dilution described, and this is from one-half to one-fourth the time required for the infusion to produce the same result.

Chopra [2] gave 0.1 Gm. per kilogram of body weight as a fatal dose for rabbits. I found that 0.01 to 0.02 Gm. per kilogram was sometimes fatal if given intravenously, and 0.0005 to 0.0010 Gm. was fatal for mice. On the other hand, a rabbit weighing 2,415 Gm. received 0.01 Gm. intravenously daily for twenty days with no evidence of harm. Merck's index gives the dose of berberine sulfate as 0.5 to 1.0 Gm. three times a day.

It is apparent, then, that berberine, while relatively nontoxic by mouth, is, like the crude infusion of algerita root, unsafe for intravenous use except in small doses.

It is interesting that the barberry family of shrubs has been used by aborigines in many parts of the world for many ailments, and this

5. Flückiger, F. A., and Hanbury, D.: Pharmacographia: A History of the Principal Drugs of Vegetable Origin Met with in Great Britain and British India, ed. 2, London, Macmillan & Co., 1879.

6. Das Gupta, B. M.: Indian M. Gaz. **65**:683, 1930.

7. Warma, J. D.: Indian M. Gaz. **66**:386, 1931.

use has been carried over into the medical profession from time to time as far back as medical history goes, but no report of an adequate investigation of the germicidal action of the substance is to be found.

As both crude infusion of Berberis trifoliatis and berberine are of low toxicity except on intravenous injection, they would seem to offer some promise, particularly for surface infections. I have used the infusion for such infections as are associated with decubitus and varicose ulcers, tonsillitis and stomatitis, and, while results are promising, more experience is required to warrant conclusions as to its value.

SURGERY OF THE GALLBLADDER IN 1910 AND TODAY

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BIRMINGHAM, ALA.

A survey of the progress and changes in the management of disease of the biliary tract during the past thirty years presents an interesting panorama.

In general, progress in medicine and surgery has been dependent to a large degree on new discoveries and improvements in the ancillary sciences. In the lifetime of the present generation probably most progress has been due to good research work by physicians themselves. The great question which agitated the surgical world from 1900 to 1910 was that of cholecystectomy versus cholecystostomy. Today it is no longer even discussed; cholecystostomy has become a rare and almost discarded operation and when employed is considered a makeshift procedure.

Certainly, the most dramatic and useful development in the diagnosis of disease of the gallbladder during this period was the introduction by Graham and his associates of cholecystography. This was first presented in 1924 and was perfected in 1925. It has since become a standard requirement in the diagnosis of biliary tissue.

It may be worth while, in order to appreciate the distance surgeons have come, to take stock of the equipment which the surgeon of 1910 had for the diagnosis and treatment of diseases of the biliary tract.

In the matter of diagnosis, the patient's history then, as today, was of paramount importance. In fact, a good history properly taken can accurately make the correct diagnosis.

A history of biliary colic, particularly if repeated, with residual soreness over the region of the gallbladder still points definitely to disease of the gallbladder. Also, slight and transient jaundice following such an attack is most suggestive. However, in the earlier period the milder degrees of cholecystitis were overlooked or were attributed to other, nonsurgical conditions. It is in detecting these early conditions and treating them that great progress has been made. If medical treatment fails to bring relief, surgical intervention can now be used safely.

The surgeon of 1910 had only poor roentgenograms, which were seldom conclusive. To his credit, he depended more on the five senses in all diagnostic work than do surgeons of today. For him there was no duodenal tube to pick up crystals of bile salts and pus from the

papilla of Vater to make the diagnosis of stone in the common duct. The van den Bergh test to help locate the origin of jaundice had not yet come to light.

Aschoff's ideas of the origin of gallstones and of the physiology of the liver have been promulgated and generally accepted. In his work on pathology he stated that there are two kinds of gallstones.

> . . . the pure cholesterol gall stone, which may occur without symptoms in a gall bladder with normal walls, and may exist in this state for a long period of time; and, as a result of the migration of organisms, or obstruction to the outlet, infection may be superimposed and inflammatory gall bladder disease result.
>
> Under the influence of inflammatory exudate of the mucous membrane, which is rich in calcium, and of the infectious decomposition of the bile, there occurs precipitation of pigment, calcium masses around the cholesterol stone, and thus originates the so-called combination stone from a nucleus of pure cholesterin, not of inflammatory origin.

Also, from his conception of bile formation has come the van den Bergh test, which indicates whether the jaundice is due to obstruction or whether it is of hematogenous origin. In most instances it is of no practical help to the surgeon.

Painless jaundice of increasing severity is nearly always due to cancer of the head of the pancreas or in the bile ducts. The work of Allen Whipple in resecting the head of the pancreas for relief of the condition is a noteworthy and recent achievement in this field.

It has long been known that the jaundiced patient is prone to bleed excessively. The surgeon of 1910 did not have the valuable weapon of transfusion to combat the menaces of hemorrhage and shock. Crile was leading the fight in giving transfusions by joining the artery of the donor to the vein of the recipient. The idea was good, but the procedure was technically futile. Jaundice was formerly believed to result almost wholly from obstructive causes resulting in back pressure on the liver. It was also believed that bile was made only by the polygonal cells of the liver.

Following the work of Aschoff and his conception of the reticulo-endothelial system, a different idea of jaundice has come about. He has stated that the Kupffer cells, which line the venous sinuses of the liver, are phagocytic, taking up hemoglobin and other detritus and turning them into bilirubin. He has also expressed the belief that the parenchymal cells merely secrete the bile and do not form it as was formerly thought. The experiments of Mann completely confirm Aschoff's theory in this matter. Today, with perfected transfusion of blood and with vitamin K, one has much better control over the bleeding and oozing of jaundiced tissues.

It is believed today that the bleeding tendency in jaundiced patients is largely due to deficiency of prothrombin in the blood. Walton stated

that the bleeding tendency from jaundice is a myth. Since vitamin K is fat soluble, it cannot be absorbed in cases of obstructive jaundice for lack of bile in the intestines. Vitamin K normally occurs in green, leafy plants, such as spinach and alfalfa.

As to blood clotting, it is believed that thromboplastin and the calcium ion unite to convert prothrombin into thrombin and also that certain amounts of thrombin will change proportional amounts of fibrogen into fibrin, thus establishing the structural basis of the clot. Since vitamin K is essential to the normal formation of prothrombin, it thus becomes an integral factor in the process of blood clotting.

Perhaps the underlying factor in reducing "surgical mortality" is the management of the body fluids, the replacing of electrolytes and of serum and blood when needed and the avoidance of alkalosis. The work of Coller and others is outstanding in this field.

The use of the Wangensteen tube has become universal and is often life saving in combating postoperative regurgitation, vomiting and distention. It has practically superseded high enterostomy, which some years ago was often performed to alleviate these symptoms.

The administration of oxygen in high concentration in the oxygen tent after operations on the gallbladder permits the patient to breathe more easily, prevents distention and is thought to guard against pneumonia.

In the matter of operative technic there has been steady progress. Gentleness in handling tissues and sharp, clean dissection have become more widespread among surgeons. Clear visualization of the bile ducts before clamping or dividing them has become general, as has knowledge of their anatomic variability.

It was not uncommon thirty years ago to see a gallbladder literally ripped from the liver, leaving a bleeding and easily infected area. Today, with subperitoneal removal, the bed of the gallbladder on the liver is left dry, smooth and clean.

However, the surgeons of 1910 were not lacking in merit or skill. One of Halsted's last contributions was the idea of exploring and draining the common duct through the stump of the cystic duct. It is a technical maneuver which has not met the acceptance which it deserves.

The methods of managing fistulas and strictures of the ducts have definitely improved.

Fortunately for patients and surgeons, the spa treatment of disease of the biliary tract practically does not exist in America, and consequently one does not encounter so many cases of advanced peribiliary involvement, such as severe chronic pancreatitis, hemorrhagic pancreatitis, chronic hepatitis and internal fistulas.

Many surgeons today are looking at acute cholecystitis in the light of acute appendicitis and are advising and performing immediate

operation. Nevertheless, the analogy is not complete, for the gallbladder rarely perforates. In a series of 350 cholecystectomies performed by me, only 1 gallbladder showed macroscopic perforation, and that occurred in a neglected diabetic patient of 72. Lahey stated that in a series of more than 1,800 cases he encountered no rupture of the gallbladder. Certainly, the early recognition and surgical treatment of these conditions prevent the advanced pathologic conditions seen in European clinics, which is reflected in an improved morbidity and mortality rate.

Not the least among the advantages enjoyed by the surgeon of today is that of modern anesthesia. Recently, the application of drugs of the sulfanilamide group to the treatment of peritonitis has shown remarkably good results, and this holds great promise. Doubtless the next thirty years will bring forth many advantages which are not on the horizon of today.

THE HUMAN SIDE OF SURGERY

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In these ultrascientific days it may possibly be construed by some as rank heresy even to suggest that there may be something else in surgery besides the purely scientific aspect. I yield to none in my admiration for those devoted men and women who have dedicated their lives and their all to science and to research into the hidden mysteries of nature. All honor to them, and may continued success attend their labors! Humanity has greatly benefited by their invaluable contributions to the sum total of human knowledge.

With no thought of detracting one iota from the credit due them, I feel constrained, however, to draw the attention of the members of the medical profession to a matter of prime importance in this connection. I believe that it will be generally accepted as a matter of common experience that as a surgeon grows older and sees more of life, particularly of the lives of his patients, and becomes better acquainted with the effect, both physical and mental, of a surgical operation on the patient, he becomes more philosophically inclined. He becomes less apt to operate by rote, as it were, and more inclined to consider each case as an individual entity and each patient as a human being just like himself and not as just one more subject to be operated on. He will, to be sure, give his patient the benefit of all that science has taught in the way of modern aseptic surgery, but even all this will not suffice for a thoughtful, observant, experienced surgeon. He will have learned after years of careful observation that there is something more in surgery than the mere mechanical carrying out of all the minute details required by the present day conception of aseptic technic; that in order to secure the best results due regard must be paid to the human element involved. It must never be forgotten that the surgical operation is being performed on a human being, whose feelings and emotions must be duly considered.

Physiologists—Cannon, Freeman, Howell and others—tell of the marked effect that emotional disturbances, such as fear or rage, may exert on the bodily functions, so marked, in fact, at times as to constitute a real menace to life itself. From the days of Hippocrates to the present time physicians have been taught that in order to secure good healing of wounds it is necessary to remove or to lessen as far as possible the effect of all factors that may exert a deleterious influence on this process. Every surgeon of experience knows how much better, as a rule, wounds heal in persons at peace and rest in mind and body. There can be little

doubt, therefore, that the state of mind in which the patient approaches an operation exerts a real influence for good or evil on its outcome. I have elsewhere called attention to the fact that a patient who, to use a common expression, is "scared to death" or who is greatly worried by gloomy forebodings as to the result of the operation or who has made up his mind that he is surely going to die is in a much less favorable condition to undergo a serious surgical procedure and make a satisfactory recovery therefrom than is one whose apprehensions and emotions are not all stirred up. As I acquire wider experience, I am more and more impressed with the advisability of the operating surgeon's paying greater attention to the mental state of the patient about to be operated on. Of course, it takes time and trouble to do this, and the surgeon's time is limited and valuable as well, so much so that he is unable or, more likely, unwilling to give up much of it to talk to and to reassure nervous or apprehensive patients concerning the nature and probable outcome of the proposed operation.

I am becoming all the time more and more convinced that it is not enough simply to inform a patient in a casual, matter-of-fact way that on a certain day at a certain hour he will be operated on and to let it go at that. The ideas current in the lay mind with regard to the discomforts, dangers and possibly unsatisfactory results inseparably connected with a surgical operation are often so erroneous and so terrifying as to constitute a real menace to the success of the operation, to say nothing of the needless mental suffering entailed. The careful, conscientious surgeon will, therefore, before undertaking any operative procedure, be sure to take the time to satisfy himself that his patient is properly informed as to just what it is proposed to do and why and also, as far as it is humanly possible to foretell, just what it is hoped to accomplish. In this way only can the degree of confidence and cooperation necessary to the fullest measure of success be established between the surgeon and the patient. But some one will say: "I haven't the time. I can operate on but half the number of patients that I do now if I spend so much time with each individual patient." The answer is simple and sure. No surgeon has the moral right to undertake to do more than he can properly accomplish.

The salutary effect that entire confidence in his physician or surgeon exerts on a patient is a matter of common knowledge and remark. Who has not met with instances in which the whole aspect of a case has been quickly changed by the effect on the morale of the patient that renewed confidence inspires? On the other hand, lack of confidence in one's physician or surgeon creates an atmosphere of suspicion and distrust, which is most unfavorable to a satisfactory outcome of any prescribed course of treatment, whether medical or surgical. As a result of these observations, I have become impressed with the fact, on which I wish to lay especial emphasis, that in preparing for a surgical operation there

is something more to be taken into account than merely the diagnosis, the aseptic technic, the administration of the anesthetic and the use of the knife, vitally important as all of these are—namely, the state of mind of the patient at the time of the operation.

It is hoped that this brief paper may direct the attention of those members of the medical profession to whose notice it may come to a phase of surgery which has hitherto not received the attention which its importance deserves; namely, the human element. Every one will agree that the surgeon has no more right to inflict needless mental anguish than he has to cause unnecessary physical pain. Both tend to lower the resistance of the patient and so render him a less favorable surgical risk. Therefore, one of the first obligations of the surgeon when he assumes the responsibility of the care of a patient is to acquaint himself with, and to remove as far as is humanly possible, all obstacles, physical and mental, to a successful conduct of the case. In order to do this satisfactorily it is essential that the surgeon should come to know as intimately as possible what the old family doctor used to call "the constitution" of his patient. Until quite recently it was customary in some circles to smile complacently when this expression was used. Now, however, its true significance is beginning to be more generally recognized.

In spite of the fact that every one who knows anything about the healing of wounds is aware of the fundamental nature of the facts just stated, how much attention does the average surgeon in his busy life pay to them? To be sure, ordinary care is usually exercised to keep the patient quiet and to relieve unnecessary pain, but that is all. Experience, however, will show that time taken to gain the patient's confidence, to remove doubts and fears from his mind, to explain just what it is proposed to do and why and what the chances of recovery of health and bodily functions are is time well spent and will yield rich returns in peace of mind, better wound healing and more rapid and complete convalescence. The *sine qua non* of the accomplishment of the best in surgery is attention to detail, mental, physical and technical. It is nothing short of the best that the surgeon should strive after in his work; it is not sufficient that it should be "good enough." It is the hundredth case that the surgeon should be constantly striving for and preparing himself to meet. This is the case the successful management of which will tax the resources of the surgeon to the utmost. The ninety-nine will probably take care of themselves either because of or (horrible thought) perhaps even in spite of whatever the surgeon may do.

Finally, in all professional efforts let there be no whit less of the scientific, but more of the human, element—more heart in all of the surgeon's relations with his patients. They will thus fare better, and he will have more real satisfaction in his work.

INTRATHECAL ADMINISTRATION OF TETANUS ANTITOXIN

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The treatment of clinical tetanus is in an uncertain and unsatisfactory state. The mortality is high; there is no agreement as to the form of treatment that gives the best results, and the therapeutic use of antitoxin has not brought about an appreciable decrease in the death rate. The explanation commonly given for this therapeutic failure is that tetanus antitoxin cannot neutralize toxin which has become fixed by the tissues. It is impossible to verify this statement in human beings, but with dogs Abel and his associates have thrown some light on the fate of tetanus toxin in the body.[1] They have shown that up to a certain time one or more lethal doses of toxin which are apparently fixed can still be neutralized if considerable excess of antitoxin is given, but if administration of antitoxin is delayed for too long a time the fixed toxin is not susceptible to the antitoxin. It has been suggested [2] that the toxin becomes altered after it is fixed in the central nervous system and that when altered it cannot be neutralized. Unfortunately, with patients there is no method by which one can ascertain (*a*) whether symptoms are due to the presence of a lethal or a sublethal amount of toxin in the body, (*b*) whether or not a lethal quantity has been fixed and (*c*) whether the fixed toxin can be counteracted by antitoxin. In treating patients, therefore, one must proceed on the assumption that a lethal amount of toxin has not become fixed and rendered unsusceptible to antitoxin.

Most physicians agree that a patient with general tetanus should be given antitoxin as soon as possible, that the wound of entrance should be widely excised even though it may appear to be well healed, that sedatives should be given and that general measures, such as rest, quiet and adequate nourishment should be provided; but here agreement stops. Some physicians still advocate treatment with phenol. There are many

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This investigation was aided by a grant from the John and Mary R. Markle Foundation.

1. Abel, J. J.; Evans, E. A., Jr., and Hampil, B.: Bull. Johns Hopkins Hosp. **59**:307, 1936.

2. Firor, W. M., and Lamont, A.: Ann. Surg. **108**:941, 1938.

articles on the use of avertin with amylene hydrate. Magnesium sulfate has an equally large and enthusiastic number of supporters. Some workers recommend administration of very large amounts of antitoxin; others say that large amounts are unnecessary. The question as to the best route for administration of the antitoxin causes the most controversy. Wainwright,[3] in 1926, stated that the quickest way to reduce mortality in general tetanus is to forbid intraspinal injection of antitoxin, and he presented statistics from which he concluded that the intravenous route is the best one. Ashhurst [4] criticized the interpretation of these statistics and strongly advised the use of the intrathecal method. From time to time every possible route of injection has been suggested, and statistical support has been offered in each instance.

Such divergence of opinion means that in actual practice no single method has been shown to be much better than another. This may be due to the fact that very few clinicians have had a sufficient number of patients to compare adequately the different methods. Since in patients one is unable to measure the amount and the condition (state of fixation) of the toxin, it is impossible to say whether a patient would survive regardless of the treatment employed. Furthermore, evaluation of clinical reports is made more difficult by the common failure to specify (*a*) the length of the incubation period, (*b*) the interval before treatment was begun, (*c*) the severity of the symptoms, (*d*) the details of the treatment, (*e*) the location of the wound, (*f*) the age of the patient, (*g*) the presence of other conditions which might have caused death and (*h*) the culture of Clostridium tetani from the wound. I have reviewed the clinical reports for the past twenty-five years and have been unable to find any basis on which to compare the results and arrive at valid conclusions. There are, however, two exceptions, those of Yodh [5] and Vener,[6] and I shall consider these in the comment at the end of the paper.

Since, therefore, the actual conditions of patients with tetanus are not accurately known, one is forced to study the disease by animal experimentation. For this paper only one of the many questions concerning general tetanus has been investigated. In combating general tetanus in a dog poisoned with two lethal doses of toxin, is the intrathecal administration of a given amount of antitoxin better than the intravenous route? It is obvious that, unlike a patient, such a dog is not continuously

3. Wainwright, J. M.: Tetanus: Its Incidence and Treatment, Arch. Surg. **12**:1062 (May) 1926.

4. Ashhurst, A. P. C.: Prognosis of Tetanus, J. A. M. A. **87**:2089 (Dec. 18) 1926.

5. Yodh, B. B.: Brit. M. J. **2**:589, 1932.

6. Vener, H. L.: California & West. Med. **48**:193, 1938.

absorbing toxin from a focus of infection; so in these experiments it is not necessary to provide a constant supply of antitoxin from repeated injections.

From time to time investigations similar to those reported in this paper have been carried out with different species of animals. Recently Shumacker, Lamont and I [7] reviewed these experiments and commented on them. A serious criticism of much of the earlier work on this subject is that treatment with intrathecal antitoxin was started before general tetanus had developed in the animals. To nullify this criticism, we compared the efficacy of the intravenous and intrathecal routes in guinea pigs and in dogs after unmistakable signs of general tetanus were present. Although these experiments [7] were carried out on a small number of animals, the results seemed to indicate a real superiority for the intrathecal route. This was true in both tetanus-sensitive animals (guinea pigs) and tetanus-resistant ones (dogs). The clinical importance of this observation made it desirable to repeat our experiments on a much larger scale and to attempt to investigate the following related problems:

1. Whether the effects of antitoxin given intrathecally are due wholly or in part to a nonspecific inflammatory reaction in the meninges.
2. Whether antitoxin introduced into the lumbar subdural space is as efficacious as that placed in the cisterna.
3. Whether it is possible to save the life of animals which are prone and convulsive with severe general tetanus.

METHODS AND MATERIALS

The tetanus toxin used in these experiments was lot no. 641-G from the Lederle Laboratory. The large amount of concentrated antitoxin used was supplied by Sharp & Dohme, Incorporated. The strength of the toxin was determined at intervals according to our usual method.[1] Lumbar punctures were made at the level of the second to the fourth lumbar segment with a shortened human lumbar puncture needle. Cisternal punctures were made with an ordinary 2 inch (5 cm.), 20 gage hollow needle. In no instance was the antitoxin injected until clear spinal fluid issued from the needle. Neither intravenous nor parenteral fluid was given to the dogs which were prone, but they were fed raw ground beef, milk and water by hand. Autopsies were performed on all dogs which died.

EXPERIMENTS

Healthy mongrel dogs were given 900 guinea pig median lethal doses (G-P LD50's) of tetanus toxin filtrate per kilogram of body weight intravenously. This was approximately two lethal doses. Fifty-three hours later the animals were divided into groups according to the severity of their symptoms and were given 680 American units of tetanus antitoxin per kilogram, either intravenously or intra-

7. Shumacker, H. B.; Firor, W. M., and Lamont, A.: Surgery, to be published.

cisternally. The results of these injections are shown in table 1. It is obvious that intracisternal administration of antitoxin is more effective than intravenous in curing early, moderate and well developed general tetanus, for of 36 dogs treated by intracisternal injections only 3 died, whereas 19 of the 25 treated by intravenous injections died. It was noted that the animals which recovered from intracisternal

TABLE 1.—*Effect of the Route of Administration on the Therapeutic Efficiency of Tetanus Antitoxin in General Tetanus in Dogs**

	Route of Administration of Tetanus Antitoxin				No Treatment with Antitoxin	
	Intracisternal		Intravenous			
Symptoms at Time of Treatment with Tetanus Antitoxin	No. of Animals	No. That Died of Tetanus	No. of Animals	No. That Died of Tetanus	No. of Animals	No. That Died of Tetanus
Early; ears erect; brows furrowed	15	1	14	8	6	6
Moderate: ears erect, brows furrowed and neck stiff	10	1	2	2	1	1
Marked: ears, brows and neck the same; slight general stiffness	8	1	9	9	..	..
Severe: generalized stiffness but animal not prone or convulsed	6	4	3	2	2	2
Total	39	7	28	21	9	9

* Each dog received 900 G-P LD50's per kilogram of tetanus toxin intravenously. Fifty-three hours later each dog treated received a single injection of 680 American units per kilogram of tetanus antitoxin.

TABLE 2.—*Effect of the Route of Administration on the Therapeutic Efficiency of Tetanus Antitoxin in General Tetanus in Dogs**

	Route of Administration of Tetanus Antitoxin					
	Intracisternal		Intravenous † Plus Horse Serum Intracisternally		Intravenous	
Symptoms at Time of Treatment with Tetanus Antitoxin	No. of Animals	No. That Died of Tetanus	No. of Animals	No. That Died of Tetanus	No. of Animals	No. That Died of Tetanus
Early; ears erect; brows furrowed	15	1	7	2	14	8
Moderate: ears erect, brows furrowed and neck stiff	10	1	..	..	2	2
Marked: ears, brows and neck the same; slight general stiffness	8	1	9	3	9	9
Severe: generalized stiffness but animal not prone or convulsed	6	4	3	3	3	2
Total	39	7	19	8	18	21

* Each dog received 900 G-P LD50's per kilogram of tetanus toxin intravenously. Fifty-three hours later each dog treated received a single injection of 680 American units per kilogram of tetanus antitoxin.

† The dogs in this group received the antitoxin intravenously and at the same time an equal amount of normal horse serum intracisternally.

injections had little or no progression of the disease. The superiority of intracisternal injections in curing severe or far advanced tetanus is not apparent in this experiment, but further investigation of this point is recorded in table 4.

Dr. LeRoy Fothergill, of the Harvard Medical School, suggested that the results of intracisternal administration of antitoxin may be due to the inflammatory reaction produced in the meninges by the serum. In an attempt to find out whether this is true, we studied a series of dogs which received tetanus antitoxin intravenously and

an equal amount of horse serum intracisternally. The data are recorded in table 2. It is clear that the combined use of horse serum and intravenous antitoxin produced better results than did the use of intravenous antitoxin alone, but the results were not so good as those obtained from intracisternal administration of antitoxin. It must be pointed out, however, that the number of animals used in this experiment was not large, and consequently the differences are correspondingly less significant.

The purpose of our next experiment was to determine whether there is any difference between the efficiency of antitoxin given intracisternally and that given in the lumbar region. The results are tabulated in table 3 and show that within the limitations of this experiment the former route is the better one except in animals with severe symptoms.

We then tried to see whether intracisternal injections of antitoxin can save an animal with far advanced general tetanus. The results are shown in table 4. We were able to save only 1 dog in the series—a dog which received the antitoxin intracisternally. We were surprised that we could save even 1, for the amount of toxin and the lapse of time before antitoxin was given were so great that we felt certain

TABLE 3.—*Comparison of Intracisternal and Lumbar Injections of Tetanus Antitoxin in General Tetanus in Dogs*

Symptoms at Time of Treatment with Tetanus Antitoxin	Route of Administration of Tetanus Antitoxin			
	Intracisternal		Subarachnoid (Lumbar)	
	No. of Animals	No. That Died of Tetanus	No. of Animals	No. That Died of Tetanus
Early: ears erect; brows furrowed	15	1	5	2
Moderate: ears and brows the same; neck stiff	10	1	15	2
Marked: ears, brows and neck the same; slight general stiffness	8	1	1	1
Severe: general stiffness; no convulsions	6	4	4	3
Total	39	7	25	8

that nothing could save the animal. It is interesting that animals given intracisternal injections survived appreciably longer than those given intravenous injections. The observation that we were able to save 1 dog with advanced general tetanus offers real encouragement in the treatment of patients critically ill with tetanus. The result of treatment in this 1 dog is not necessarily inconsistent with our view that when a lethal amount of toxin has been fixed and altered no amount of antitoxin avails to save the animal's life, for Abel has shown that severe symptoms of generalized tetanus may occur when sublethal amounts of toxin are given. It is likely that when treatment was begun for this particular dog a lethal quantity was not yet fixed in the central nervous system. This experiment is of sufficient importance to justify a brief account.

Each dog received one lethal dose (480 G-P LD50's per kilogram) of tetanus toxin intravenously. As the dogs became prone and exhibited frequent convulsions they were assigned alternately to one of three groups. One group received antitoxin intracisternally; one group received antitoxin intravenously, and the third group received no antitoxin. The animals in the first two groups were given 1,300 units of antitoxin per kilogram at each injection. If the animals survived, these injections were repeated at approximately twenty-four hour intervals to a total of five.

In table 5 we have summarized all the antitoxin experiments carried out on dogs in our laboratory. This table includes animals which were given 480 to 2,400 G-P LD50's of toxin per kilogram. They were treated at various stages of the disease (from forty-eight to one hundred and sixty-eight hours after introduction of the toxin). Some animals received as little as 1 unit of antitoxin per kilogram, whereas

TABLE 4—*The Treatment of Advanced General Tetanus in Dogs*

Route of Administration of Tetanus Antitoxin	Number of Dogs	Number of Deaths	Average Time of Death in Hours: After Injection of Toxin	Average Time of Death in Hours: After Onset of Symptoms
Intracisternal	4	3†	163*	41*
Intravenous	4	4	145	22.6
Control—no tetanus antitoxin	5	5	124	8.5

* The animal which survived is not included in these figures.
† A brief protocol of the surviving animal follows:
March 12, 11 a. m. Received toxin (2,500 G-P LD50's)
14 Beginning erection of ears
16, 11 a. m. Trismus, stiff body; questionable distemper
6 p. m. Prone; clonic convulsions; received 67,600 American units of antitoxin intracisternally
18, 10 a. m. Condition the same; received same dose of antitoxin
19, 10 a. m. Condition the same; received same dose of antitoxin
20, 11:30 a. m. Condition the same; received same dose of antitoxin
21, 10:30 a. m. Condition the same; received same dose of antitoxin
22 No longer having convulsions; can drink; still prone and stiff; has external opisthotonos. The dog gradually recovered.

TABLE 5.—*Effect of the Route of Administration on the Therapeutic Efficiency of Tetanus Antitoxin in General Tetanus in Dogs**

	Route of Administration of Tetanus Antitoxin: Intracisternal	Subarachnoid (Lumbar)	Intravenous Plus Horse Serum Intracisternally	Intravenous	No Treatment with Antitoxin
Total number of animals	70	30	20	65	21
Number of deaths	24	11	9	52	21
Number of animals that died of tetanus	17	11	8	47	21
Number that probably died of tetanus, although other pathologic conditions were present	2	..	1	2	..
Number that died of other causes, having had no progression of the tetanus	5	..	..	3	..
Gross mortality	34%	37%	45%	80%	100%
Mortality from tetanus	27%	37%	45%	75%	100%

* The dogs received from 480 to 2,400 G-P LD50's per kilogram of tetanus toxin intravenously. The dogs treated received from 1 to 2,400 American units of tetanus antitoxin at intervals of from 48 to 168 hours after the injection of the toxin.

the maximum amount given was 2,400 units per kilogram. It will be seen that if one excludes animals dying from other causes than tetanus, the mortality in the 70 dogs which received the antitoxin intracisternally was 27 per cent. In the 30 dogs treated by lumbar injection the mortality rate was 37 per cent. In the 20 dogs given antitoxin intravenously and horse serum intracisternally the death rate was 45 per cent, and in those treated solely by the intravenous route the mortality rate

was 75 per cent. All the animals not treated died of tetanus. According to these figures the superiority of the intrathecal route is not so great as it is in the treatment of dogs suffering from early and moderately severe tetanus, yet they furnish conclusive evidence that the mortality among dogs dying from general tetanus is lowest when the antitoxin is administered intracisternally.

COMMENT ON CLINICAL REPORTS

Clinicians have been sharply divided as to the desirability of giving tetanus antitoxin intrathecally. Wainwright,[3] Gage and DeBakey [8] and many others have advised against its use. Golla [9] and Calvin and Goldberg [10] stated that no conclusions can be drawn from their experience as to whether subdural injection of antitoxin is better than other methods of treatment. Many authors have strongly advocated this form of treatment. Recently Vener [6] has described 75 consecutive patients treated with intracisternal injections, with a gross mortality of only 26.6 per cent. When he omitted the patients who died within twenty-four hours after admission to the hospital, the mortality was only 16.6 per cent. It is difficult to derive sound conclusions from the clinical reports as to the best method of treatment, for the groups treated in the various ways are not capable of being compared. Frequently authors have failed to specify the length of the incubation period, the interval before treatment, the severity of the disease when treatment was begun and the details of the treatment. Besides the encouraging report of Vener, there has been published a paper of particular significance by Yodh, who treated 214 patients with tetanus in a group of 263 who were seen during a relatively short period. He divided these patients into three groups and presented evidence to show that they were approximately the same with reference to the length of the incubation period, the absence or presence of a history of injury and the presence of a septic wound. In the first group, 49 consecutive patients received small doses of antitoxin (20,000 units) intravenously or intramuscularly. Three of these patients also were given "lumbar subarachnoid injections." In this group there was a gross mortality of 77.5 per cent cent, which was lowered 10 per cent when those patients who died within twenty-four hours after admission were excluded. In the second group, 102 patients were given larger doses of antitoxin (averaging about 40,000 units) by the intravenous or the intramuscular route. The gross mortality was 65 per cent, and when the patients who died within twenty-four hours after admission were omitted, this rate fell to 50 per cent. Finally, the last 112 patients received the same amount of antitoxin as those in the second group, but

8. Gage, M., and DeBakey, M.: South. Surgeon **4**:246, 1935.

9. Golla, F.: Lancet **2**:966, 1917.

10. Calvin, J. K., and Goldberg, A. H.: Prognosis of Tetanus, J. A. M. A. **94**:1977 (June 21) 1930.

all of them were given it intracisternally as well as by other routes. The gross mortality was 46.5 per cent, and when the patients who died within the first twenty-four hours were left out this figure fell to 23.4 per cent.

Recently Dietrich [11] has described the clinical picture of children dying from severe reactions following intravenous or intracisternal injections of antitetanic serum. He stated that "it resembles certain phases of bulbar poliomyelitis, or some other disease with medullary pressure or edema." In none of our animals has such a reaction occurred, nor has Vener reported fatal reactions in any of the 75 patients he treated by intrathecal injections of antitoxin. Dietrich's report contains no information as to the quantity of serum used, the rate of administration, the dilution of the injected antitoxin or the source of the serum. He stated, however, that "the refinement of serums in the last few years has probably aided in reducing the number of severe reactions." It is our feeling that Dietrich's observations give a timely warning against injudicious injection of antitetanic serum but that his data do not justify the abandonment of intravenous or intrathecal administration of antitoxin.

GENERAL COMMENT

The experiments which form the basis of this paper indicate clearly that in the treatment of dogs with mild or moderately severe tetanus intracisternal injections of antitoxin are far more effective than intravenous ones. These experiments in themselves do not warrant the use of intracisternal injections for patients, but when considered with the clinical reports of Yodh or Vener they furnish a strong argument for the employment of this form of treatment. It is highly desirable that a more refined antitetanic serum be produced in order to minimize the severe reactions described by Dietrich. This may possibly be accomplished in one of two ways. First, ordinary antitetanic horse serum may be concentrated and purified by the action of proteolytic enzymes, as has been done with diphtheria antitoxin.[12] Secondly, human serum containing a high titer of tetanus antitoxin may be produced by active immunization of human donors with tetanus toxoid. This possibility was first suggested, as far as I know, by Dr. Clarence Hyland, of the Serum Center of the Children's Hospital in Los Angeles. Our experiments comparing the efficacy of intracisternal and lumbar routes are suggestive but not conclusive. Had we kept the animals in a position to cause a gravitational flow of the serum to the medulla, the apparent difference in results with the two sites of injection might have disappeared. Similarly, we do

11. Dietrich, H. F.: Tetanus in Childhood, with Special Reference to Treatment, Am. J. Dis. Child. **59**:693 (April) 1940.

12. Pope, C. G.: Brit. J. Exper. Path. **19**:245, 1938.

not consider that our experiment, which was designed to evaluate the importance of the inflammatory reaction to foreign serum in the meninges, is conclusive. Additional studies with purified serum on a larger number of animals are necessary before this question can be settled.

SUMMARY

Experiments are recorded which show that the intracisternal injection of antitoxin into dogs suffering from early, mild or moderately severe tetanus yields far better results than intravenous injection. In animals with severe tetanus there is little difference in the results obtained by the various routes of administration of antitoxin, but the difference that occurs favors the intracisternal route.

Dr. Austin Lamont and Dr. Harris B. Shumacker Jr. assisted in the performance of these experiments.

ORIGIN, EVOLUTION AND SIGNIFICANCE OF GIANT CELLS IN RIEDEL'S STRUMA

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The occurrence of giant cells or so-called pseudo giant cells with the chronic nonspecific thyroiditis usually designated as Riedel's struma has been frequently noted since Riedel [1] described this disease in 1896. In his original report, however, no mention is made in the microscopic observations of the presence of giant cells. In a considerable number of subsequent reports the occurrence of giant cells in Riedel's struma has been noted, but few studies have been made with the particular purpose of determining their mode of origin and evolution, their possible function, if any, and their ultimate fate. As a result they are little understood, and various unsubstantiated views have been expressed regarding their origin and significance. The most common misconception regarding their nature is that they are foreign body giant cells possessing phagocytic properties. One unfortunate result of this assumption has been to bestow on them a significance which cannot aid in an ultimate understanding of the etiologic factors and the true pathologic processes at work in the destruction of the thyroid gland associated with Riedel's struma. Furthermore, the presence and supposed phagocytic function of the giant cells described in many previous reports have led to mistaken diagnoses of tuberculosis, syphilis and carcinoma and to consequent misdirected therapy. A recent case of Riedel's struma is presented, together with the pathologic observations in the thyroid gland, particularly as they relate to the giant cells, which were present in large numbers. It is my purpose to interpret these observations, which are similar to those previously made in a considerable number of personal cases, with the hope that the evidence submitted will clarify the true nature of the giant cells and thus eliminate one element of confusion in understanding of the basic pathologic processes at work in this disease. One should thereby approach somewhat nearer to the cause of this condition.

From the Departments of Surgery of the Long Island College Hospital and the Long Island College of Medicine.

1. Riedel, B.: Die chronische, zur Bildung eisenharter Tumoren führende Entzündung der Schilddrüse, Verhandl. d. deutsch. Gesellsch. f. Chir. **25**:101, 1896.

REVIEW OF LITERATURE

Wilke [2] was one of the few authors who concerned himself specifically with the origin and function of the giant cells associated with chronic nonspecific thyroiditis of the Riedel type. He noted the occurrence of giant cells supposedly produced by irritation of the colloid acting as a foreign body and described the apparent erosion of the colloid by them. At times the giant cells were described as completely encircling a globule of colloid. He expressed doubt that the giant cells are formed by coalescence of follicular cells and implied that their origin is analogous to the formation of giant cells in the prostate, which he described as follows: The follicular lining cells disappear as a result of pressure atrophy produced by the foreign body (concretions in the prostate and colloid in the thyroid), whereupon the foreign body exerts a stimulating or irritative action on the periacinar fibrous tissue with the resultant formation of giant cells. He noted that as long as the follicular lining is intact and the foreign bodies lie free in the lumen no giant cells are formed.

Creite [3] was influenced to regard as tuberculous the thyroid glands in 2 instances of apparently typical Riedel's struma because of the occurrence of intrafollicular epithelial giant cells not unlike those associated with Riedel's struma. In fact, he designated them as intrafollicular tubercles. This diagnosis was made in spite of freedom from tuberculosis elsewhere, the fact that the patients had completely recovered from operation and were entirely well five to five and one-half years later and the absence of necroses or typical tubercles.

A common conception has been that the giant cells are formed in response to foreign body irritation and possess phagocytic properties. Thus Reist [4] reported 6 cases of Riedel's struma, in 1 of which he described epithelial giant cells in contact with, or surrounding, masses of colloid in a manner analogous to foreign body giant cells. These cells were further described as sending out radiating offshoots into the colloid and thus possibly represented the beginnings of true giant cells.

Graham and McCullagh [5] reported 4 cases of struma lymphomatosa (Hashimoto), a condition in some respects analogous to Riedel's struma, in 3 of which they noted the occurrence of giant cells of the foreign body type which were phagocytosing not only the colloid engulfed by

2. Wilke: Ueber Riesenzellenbildung in Thyreoidea und Prostata, Virchows Arch. f. path. Anat. **211**:165, 1913.

3. Creite, C.: Ueber tuberkulöse Strumen, Beitr. z. klin. Chir. **78**:487, 1912.

4. Reist, A.: Ueber chronische Thyreoiditis, Frankfurt. Ztschr. f. Path. **28**: 148, 1922.

5. Graham, A., and McCullagh, E. P.: Atrophy and Fibrosis Associated with Lymphoid Tissue in the Thyroid (Struma Lymphomatosa Hashimoto), Arch. Surg. **22**:548 (April) 1931.

them but the epithelial cells. By means of injections of alcohol into the thyroid gland of the dog Olper [6] produced epithelial giant cells derived from the follicular cells and resembling those seen in Riedel's struma. He regarded them as resulting from foreign body irritation by the colloid, on which they were stated to have a phagocytic action. Joll [7] emphasized what he stated to be the rare presence of foreign body giant cells in Riedel's struma as compared with Hashimoto's disease and stated that the role of these cells is elimination of the colloid which cannot otherwise be absorbed.

A further view has been that giant cells are formed by fusion of epithelial cells into protoplasmic masses which have phagocytic power. Thus Kreuzbauer [8] reported the observation of giant cells filled with colloid and apparently formed by the fusion of epithelial cells around degenerating colloid droplets, giving thus the appearance of foreign body giant cells whose function might be that of splitting up the colloid. Lee [9] noted the occurrence of multinucleated giant cells in 8 of the 9 instances of Riedel's struma reported by him and stated that these giant cells had an appearance strongly suggestive of fusion of follicular epithelial cells around droplets of colloid on which they probably exerted a phagocytic action, as indicated by their assumed content of colloid droplets. In 19 cases of atrophy and fibrosis of the thyroid gland (Riedel's struma) collected from the literature from 1930 to 1937 and in 4 personal cases McClintock and Wright [10] reported the occurrence of foreign body giant cells to which they attributed phagocytic properties without recording evidences for this assumption. Eisen [11] reported from my service 7 instances of Riedel's struma in which he noted the occurrence of multinucleated cells which he designated pseudo giant cells, in apparent distinction from the true Langhans type of giant cell, which he very rarely observed. He thought he recognized two types of giant cells, one formed of a mass of colloid with desquamated cells arranged about its periphery and the other composed of a cluster of epithelial cells that had lost their cell definition and formed pseudo giant cells containing many nuclei.

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6. Olper, L.: Riproduzione sperimentale di cellule giganti epiteliali nelle tiroide, Sperimentale, Arch. di biol. **89**:555, 1935.

7. Joll, C. A.: The Pathology, Diagnosis and Treatment of Hashimoto's Disease (Struma Lymphomatosa), Brit. J. Surg. **27**:366, 1939.

8. Kreuzbauer, F. H.: Die Thyreoiditis chronica. Ein Beitrag zur Kenntnis der Riedelschen "eisenharten Struma," Arch. f. klin. Chir. **163**:86, 1930.

9. Lee, J. G.: Chronic Nonspecific Thyroiditis, Arch. Surg. **31**:982 (Dec.) 1935.

10. McClintock, J. C., and Wright, A. W.: Riedel's Struma and Struma Lymphomatosa (Hashimoto), Ann. Surg. **106**:11, 1937.

11. Eisen, D.: Riedel's Struma, Am. J. M. Sc. **192**:673, 1936.

REPORT OF A CASE

F. A., an American housewife aged 52 (fig. 1), was admitted to the Long Island College Hospital Dec. 4, 1939, complaining of enlargement of the neck and a feeling of tightness of the throat, nervousness, tremor and easy fatigue. She was the mother of two healthy children. Her general health had always been good. She had had amenorrhea since oophorectomy and partial hysterectomy performed four years prior to entrance. During the six years prior to her admission to the hospital she had been subject to attacks of sneezing and lacrimation due to some form of allergy. Fifteen years before entrance she was told that she had an enlargement of the thyroid affecting principally the right side. She was treated with iodine, with some apparent benefit. At the same time she suffered with nervousness. During the succeeding years her nervous condition improved, but

Fig. 1.—Photograph showing fulness of the neck due to diffuse enlargement of the thyroid gland (Riedel's struma).

she was always cognizant of a "lump" on the right side of her throat. A tickling, hacking cough, some huskiness of the voice and considerable clearing of the throat had been noted for a number of years. At no time had she suffered pain in the region of the thyroid, and there was no difficulty in swallowing. There had been occasional periods of transient aphonia after considerable use of her voice. Slight edema of the eyelids was often noted, but there was no protrusion of the eyes. A tremor had been noted for five or six years. There was no family history of goiter. The menses began at the age of 13 years and were always normal. The bowels were constipated. During the year previous to examination she was particularly conscious of nervousness, irritability and throbbing of the heart. Her greatest weight two years prior to examination was 186 pounds (84.5 Kg.). Her weight on admission was 168 pounds (76 Kg.), the loss of 22 pounds (10 Kg.) being

attributed largely to restriction of diet. She had paid little attention to her thyroid condition until four weeks prior to admission, when she suffered an attack of "grip and head cold," after which the swelling in her neck enlarged and became definitely tender. She became fatigued more easily, and the sensation of constriction of her throat increased.

Examination showed her to be well developed and well nourished. The skin of the neck and upper part of the chest was flushed and presented a reddish, mottled appearance. A faint, wheezing "tracheal" sound was heard on deep inspiration. The eyes were bright and had a staring expression, but there was no definite exophthalmos. Slight edema of the lower lids was noted. The pupillary reactions were normal. Examination of the mouth, throat and cervical lymph glands revealed no abnormality. The neck (over the thyroid swelling) measured 34.5 cm. in circumference. A diffuse, moderate prominence of the thyroid gland was noticeable, the greatest prominence being on the right side. The overlying skin was freely movable; on palpation the isthmus was found to be broadened and thickened; the lobes of the thyroid were unusually firm and resistant, moderately full and not tender, and their surfaces were slightly uneven. The gland preserved its normal contour and appeared to be closely encircling the trachea. Discrete nodules were not felt. A slight pulse was noted over the poles of the gland, but no definite thrills or bruits were detectable. A thin, rather firm pyramidal lobe was felt. The Chvostek sign was negative. There was a slight tremor of the extended fingers. The skin was somewhat dry, and the hands and feet were cold. All reflexes were active. The pulse rate was 102, and occasional extrasystoles were noted. The temperature and respiratory rates were normal. The heart sounds were of good quality and regular. The abdomen showed a scar low in the midline but was otherwise normal. The basal metabolic rate on December 5 was +12 per cent. The systolic blood pressure registered 162 and the diastolic 120 mm. of mercury. The blood, urine and blood chemistry were normal.

The clinical diagnosis of Riedel's struma or possibly Hashimoto's disease was made. Operation was advised, and preoperative administration of iodine was omitted.

Operation.—Removal of the isthmus and the pyramidal lobe and partial bilateral resection of the lobes of the thyroid were performed by me on December 6. Cyclopropane anesthesia was employed. A low collar incision was made, whereupon the subcutaneous tissues were seen to be unusually vascular. Dense adhesions were noted between the pretracheal muscles which, in turn, were adherent to the capsule of the thyroid gland, exposure of which was therefore somewhat difficult. The surface of the thyroid presented a mottled pinkish white appearance. A thickened isthmus and a small, firm pyramidal lobe were noted. The gland was five or six times the normal size; it was unusually firm and resistant, and the surface vessels were moderately well defined but were not elevated above the surface. Considerable extracapsular fibrosis, the fibrous tissue partially enclosing the large vessels of the neck, was noted. The thickened isthmus and a small, firm, whitish pyramidal lobe were adherent to the trachea, from which they were separated without great difficulty. On transection a creaking, gristly feeling was imparted to the hand. A bluish, thin-walled adenoma the size of a small olive was enucleated from the right upper pole. A tan nodule in the middle of the lobe and another in the lower pole gave the appearance of a circumscribed area of old gland. A restricted, partial resection of the right lobe was done, a generous residue being left toward the middle and lower portions of the lobe. A cystic cavity the size of a large pea, containing hemorrhagic fluid, was encountered. Extensive areas of dense, white

fibrous tissue enclosing minute areas of light brownish gland and larger areas of atrophic-appearing gland were noted. The cut surface bled freely, requiring many fine silk sutures for the control of hemorrhage. Thereupon about one third of the left lobe was resected, a generous residue remaining. A lobulated colloid adenoma of the left lower pole, about the size of a hazelnut, was enucleated. The remaining stump was reconstructed with fine silk. A fairly large artery supplying the right half of the isthmus on the right side and the arteries at both poles of the gland appeared sclerotic. Throughout the operation there was a tendency to continuous oozing of blood from cut surfaces.

A fundamental hypersensitivity to operation, persisting from probable previous hyperthyroidism, was noted in the definite blood pressure response during operation, the systolic pressure rising to 236 mm. of mercury and subsiding to 158 mm. at the end of the operation. There was a mild rise in the diastolic pressure. The pulse rate in the afternoon following operation was 85. On the day after operation the highest temperature was 99.6 F. The convalescence was normal.

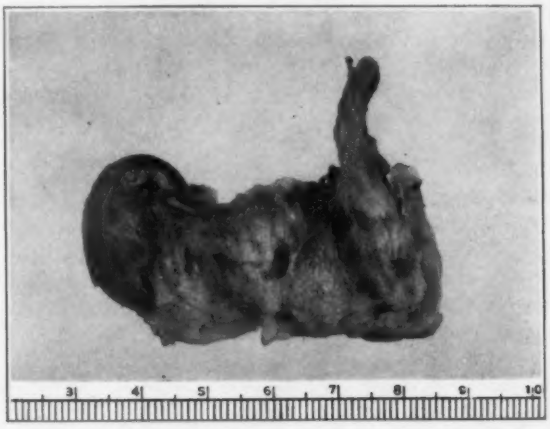

Fig. 2.—Photograph of the pyramidal lobe, the isthmus and the resected portion of the right lobe of the thyroid. Note the oval adenoma at the left border of the specimen.

The patient was discharged in good condition on December 16, ten days after operation. The wound was thoroughly healed. The basal metabolic rate ten days after operation was + 3 per cent.

Pathologic Examination.—The tissue removed at operation weighed approximately 21 Gm. and consisted of a fairly large section of the right lobe of the thyroid together with the isthmus, the pyramidal lobe and a small section of the left lobe. The larger specimen measured 5.5 by 2.5 by 2 cm. The pyramidal lobe was 2 cm. in length and 0.6 cm. in thickness. The resected portion of the left lobe with a margin of isthmus measured 1 by 1 by 3 cm.

Gross Description: The resected specimen (fig. 2), which was whitish, had preserved the normal surface contour of the thyroid. The thickened capsule showed superficial irregularities; the vessels were distinct, and the gland was everywhere unusually dense, firm and slightly resilient.

On the glistening, freshly cut surface could be seen broad, dense bands of interlacing white fibrous tissue enclosing small irregular areas of light brown, atrophic-

appearing thyroid tissue. In the center of the specimen from the right lobe there was a discrete nodule of light brown colloid thyroid gland measuring 2 by 1.5 cm. in diameter, and in the right upper pole a discrete encapsulated nodule measuring 2.5 by 2 by 1.5 cm. was noted (fig. 2). On transection this nodule showed a thin, white fibrous capsule enclosing a gelatinous tissue consisting of small colloid cysts and distended acini. In the center of the nodule a large brownish blood clot was seen. Fibrous tissue was strikingly absent in this nodule, which presented a remarkable contrast with the dense fibrous tissue partially surrounding it. The resected portion of the left lobe presented a dense, whitish appearance and a general structure similar to that described for the right lobe. Here also small areas of tan-colored isolated islands of thyroid parenchyma and one small colloid adenoma were seen embedded in the fibrous stroma. The pyramidal lobe was firm, irregular and whitish. The left superior thyroid artery and its branch to the isthmus appeared sclerotic.

Microscopic Description: Sections were made from a block comprehending the entire vertical length of the resected portion of the left lobe of the thyroid. One was selected because of its characteristic pathologic features, which were representative of those in many other areas of the resected gland. The following stains and procedures were employed in the preparation of the sections: hematoxylin and eosin; Bensley's[12] "acid fuchsin–methyl green" method for the demonstration of mitochondria; Mallory's technic for staining fibrous tissues, and sudan III for the study of fat.

The results of low power study were as follows: Examination of the periphery of the section showed the capsule to be enormously thickened and composed of hyalinized fibrous tissue containing numerous minute blood vessels. At one end, corresponding to the upper pole of the thyroid, large, thick-walled vessels were seen. The striking feature of the section was the enormous increase in hyalinized, sparsely nucleated fibrous tissue arranged in broad anastomosing bands which divided the thyroid parenchyma into large and smaller isolated islands. The large islands appeared to be lobules of gland, and the smaller islands appeared to be the result of subdivision of lobules by the penetration of smaller strands of fibrous tissue. In the larger islands the acini varied greatly in size, from minute (with a droplet of colloid) to moderate; in the smaller islands the acinar character of the thyroid parenchyma was almost wholly lost.

The results of medium high power study were as follows: Small focal accumulations of lymphoid cells, without germinal centers, surrounding small blood vessels were noted immediately under the capsule and here and there throughout the section, particularly in the islands of isolated parenchyma. Some of the larger islands were composed of lobules of gland consisting of minute and moderate-sized acini and separated by small bands of hyalinized connective tissue. The acinar colloid was stained faintly red. The follicular lining, composed of low cuboidal or flat cells, was smooth. The nuclei were rounded, were of uniform size and contained a moderate amount of chromatin. In the relatively normal-appearing areas of thyroid tissue there was an absence of lymphoid cell infiltration; the stroma was not unusually cellular, and the interfollicular small vessels were congested. The generally cellular stroma, composed of dense fibrous tissue, encircled and isolated many small islands of thyroid parenchyma hardly recognizable as such. There was a considerable increase in the interacinar hyaline fibrous tissue, which contained numbers of lymphocytes. The blood vessels were small and hardly perceptible.

12. Bensley, R. R.: Studies on the Pancreas of the Guinea Pig, Am J. Anat. **12**:308, 1911.

The acini, some of which were empty while others contained globules of colloid, were of small and medium size. They were lined by either flat or cuboidal epithelium or had almost completely lost their identity. Here and there in these isolated islands a few acini were seen, which appeared active in that the lining cells, provided with large, rounded, well stained chromatic nuclei, were large and low columnar, with granular protoplasm devoid of vacuoles or other evidences of degeneration. In many of the acini the large follicular cells, with pink-staining,

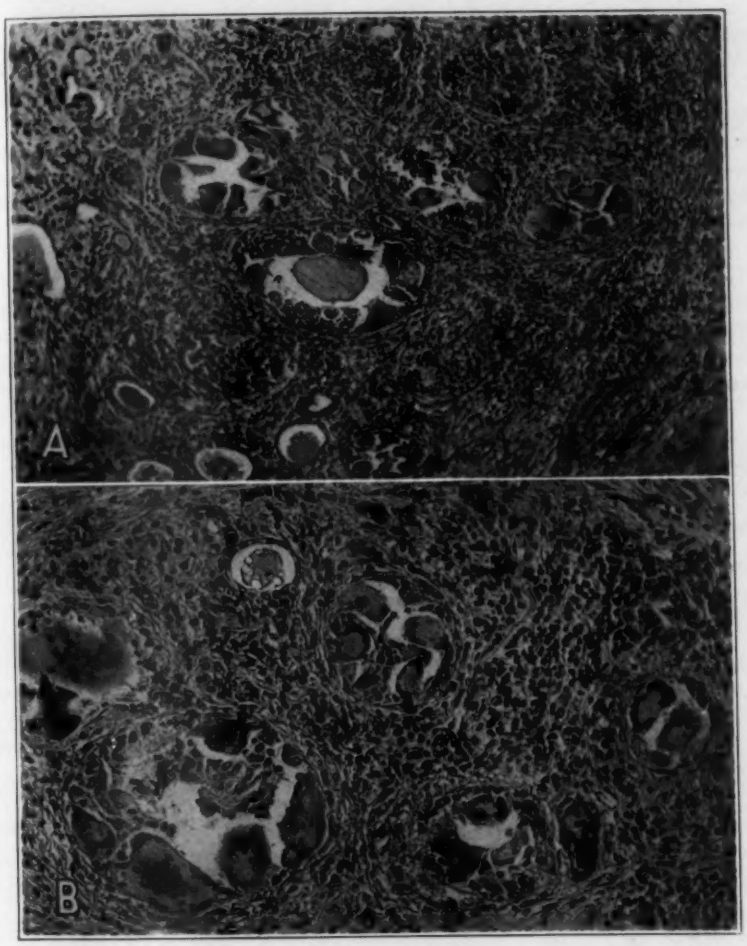

Fig. 3.—Photomicrographs of representative sections, *A* (× 85) and *B* (× 150), from the left lobe of the thyroid, showing desquamated follicular epithelial cells which have fused to form multinucleated, protoplasmic masses (giant cells). Various stages in progressive degeneration of the giant cells are illustrated. Note the similarity in appearance of the protoplasm of the giant cells seen in *B* and the follicular colloid shown in *A*. Only an occasional atrophic follicle remains in the cellular, fibrous stroma typical of that found in Riedel's struma. (Hematoxylin and eosin.)

granular cytoplasm, had separated from their basement membranes and were desquamating into the lumens. In this process the follicular cells had often fused into syncytial masses of granular protoplasm containing eight to ten or more dark-staining nuclei. In other acini the desquamated cells had arranged themselves around the periphery of the acinar colloid. Thus in both instances the resultant appearances simulated early stages in the formation of giant cells. In some of the acini the colloid contained discrete desquamated cells which were undergoing fatty degeneration.

The results of high power study were as follows: Islands of atrophic and degenerating thyroid follicles were demarcated by interacinar fibrous stroma in which groups of thyroid cells were still recognizable, though they had lost their acinar character. However, the striking feature was the occurrence of large numbers of medium-sized follicles, the large lining cells of which had desquamated from the basement membranes and had coalesced into definitely granular, nonvacuolated, pink-staining masses of multinucleated protoplasm. The closely aggregated nuclei were large, vesicular, round, oval or irregular and contained small amounts of granular chromatin and fairly well defined nucleoli. Occasionally the nuclei of these desquamated cells had completely circumscribed the acinar globule of colloid. In the interstices of the interacinar hyaline connective tissue there were numerous lymphoid and epithelioid cells. There were a few elongated connective tissue cells and occasional plasma cells. Rare polymorphonuclear and a few granular eosinophilic cells were seen. In the stroma between the larger acini, minute, active-appearing thyroid acini composed of cells with columnar, nonhydropic, granular protoplasm could be seen. These acini were often empty or contained a mere droplet of colloid. Other thyroid cells, in groups, had lost their follicular arrangement and appeared atrophic. The capillaries were congested and few.

The following transitional stages in the formation and degeneration of the giant cells (figs. 4 and 5) could be clearly recognized: separation of follicular cells from their basement membranes and coalescence of the protoplasm and nuclei of neighboring cells into multinucleated syncytial masses; disappearance of the acinar colloid; shrinkage of the protoplasmic masses with conglomeration of the nuclei and formation of typical-appearing "giant cells"; the loss of acinar identity as a result of ingrowth into the lumen of undifferentiated cells derived from the limiting fibrous membrane of the follicle completely surrounding the atrophic giant cells, and finally the virtual disappearance of the protoplasm of the giant cells and karyorrhexis of their nuclear aggregates, which then were hardly recognizable in a maze of undifferentiated cells and fibrous tissue. Details of formation, degeneration and final disappearance of the giant cells were as follows:

At the beginning the follicles were partly or completely filled with pink-staining, homogeneous colloid and were lined by active-appearing cuboidal cells with granular protoplasm. The nuclei were rounded or oval and densely stained (fig. 4 *a*). The colloid was often shrunken away from the lining cells.

Occasional follicles were noted in which all or the majority of the large follicular cells had separated from their basement membranes, incidentally losing their individual cell definitions. They had fallen in the lumens and thereupon, by mere accident, surrounded a central mass of colloid (fig. 4 *b* and *c*). The protoplasm of these rather large cells appeared finely granular and nonvacuolated, and the nuclei were rounded or oval and appeared swollen. They were relatively clear because of the small amounts of chromatin which they contained. In places the basement membrane of the follicle was devoid of cells; at other points multinucleated protoplasmic crescents were seen still clinging to it. In some areas,

where the follicular lining cells had desquamated, there was replacement by several layers of undifferentiated cells derived from the basement membrane and infiltrated between the protoplasmic masses (fig. 4 *d* and *f*).

Other follicles were then noted in which the desquamated cells had fused into small syncytial masses of pink-staining protoplasm containing large numbers of fine granules (mitochondria). The nuclei of these fused cells arranged themselves peripherally about masses of protoplasm, thus simulating the appearance of small thyroid acini (fig. 4 *e*). In some instances the compact nuclei were embedded in small, conglomerate masses of protoplasm (fig. 4 *f*). Central globules of homogeneous-appearing colloid were occasionally seen to be quite isolated from the adjoining masses of fused follicular cells (fig. 4 *c*). There was no evidence of phagocytic activity by these protoplasmic masses, which did not contain colloid droplets or cellular debris. The adjoining colloid similarly failed to give any appearance of being phagocytosed (fig. 4 *b* and *c*). The nuclei of the syncytial, protoplasmic masses appeared fairly large; they were rounded, oval or irregular and contained a relatively scant amount of chromatin. In several acini layers of undifferentiated nonepithelial cells had overgrown the basement membranes and were infiltrating the protoplasmic masses (fig. 4 *f*).

A further stage of transition was noted in the coalescence of these protoplasmic clumps into irregular, bizarre, syncytial masses containing twenty or thirty closely aggregated pyknotic nuclei (fig. 5 *g* and *h*). The protoplasm appeared coarsely and finely granular and without vacuoles, colloid or cellular debris. The appearance now approached that of huge giant cells (fig. 5 *h*, *i* and *j*). The central globule of acinar colloid, when present, appeared homogeneous, in distinct contrast with the granular protoplasm of the giant cells, which gave no appearance of phagocytosing the colloid. Often the nuclei, which were in many layers, arranged themselves in crescents bordering one side of the lumen (fig. 5 *j*).

In the further evolution of these syncytial giant cell masses it was noted that their protoplasm was becoming scantier but that in most instances its finely granular character was preserved. In rare instances the protoplasm contained lipoid globules. The central small mass of protoplasm with peripherally situated nuclei gave the appearance of minute acini (fig. 5 *k*). The colloid had disappeared. The original follicles were still defined by the basement membranes, which were faintly visible (fig. 5 *k* and *l*). Some of these small acini were overgrown by masses of compact, undifferentiated cells with scanty, nongranular protoplasm and oval, rounded or irregular, deeply stained nuclei. This undifferentiated, nonepithelial tissue, in which the giant cells could be readily distinguished, partially or completely filled the follicle, thus incidentally surrounding the giant cells (fig. 5 *k* and *l*). Here again there was no evidence of phagocytic activity on the part of the giant cells, the protoplasm of which showed no inclusions of foreign material.

Other syncytial giant cell masses were then noted, in which increased numbers of fat droplets began to appear and in which shrinkage and partial disappearance of the protoplasm had occurred, with consequent coalescence of surviving nuclei into dark-staining, dense, pyknotic nuclear aggregates. From ten to thirty nuclei could be counted in a single giant cell (fig. 5 *j*, *k* and *l*). The nuclei were oval and atrophic appearing and contained finely granular, poorly staining chromatin. The outlines of the follicle could scarcely be recognized, because the lumen had been completely filled with undifferentiated cells, embedded in which the easily recognized nuclear aggregates of the giant cells could be seen (fig. 5 *l*). Finally the identity of the follicles was almost or wholly lost. The giant cells at this stage were almost devoid of protoplasm, and that remaining was spongy, nongranular and poorly stained and contained numerous fat droplets (sudan III). The pyknotic

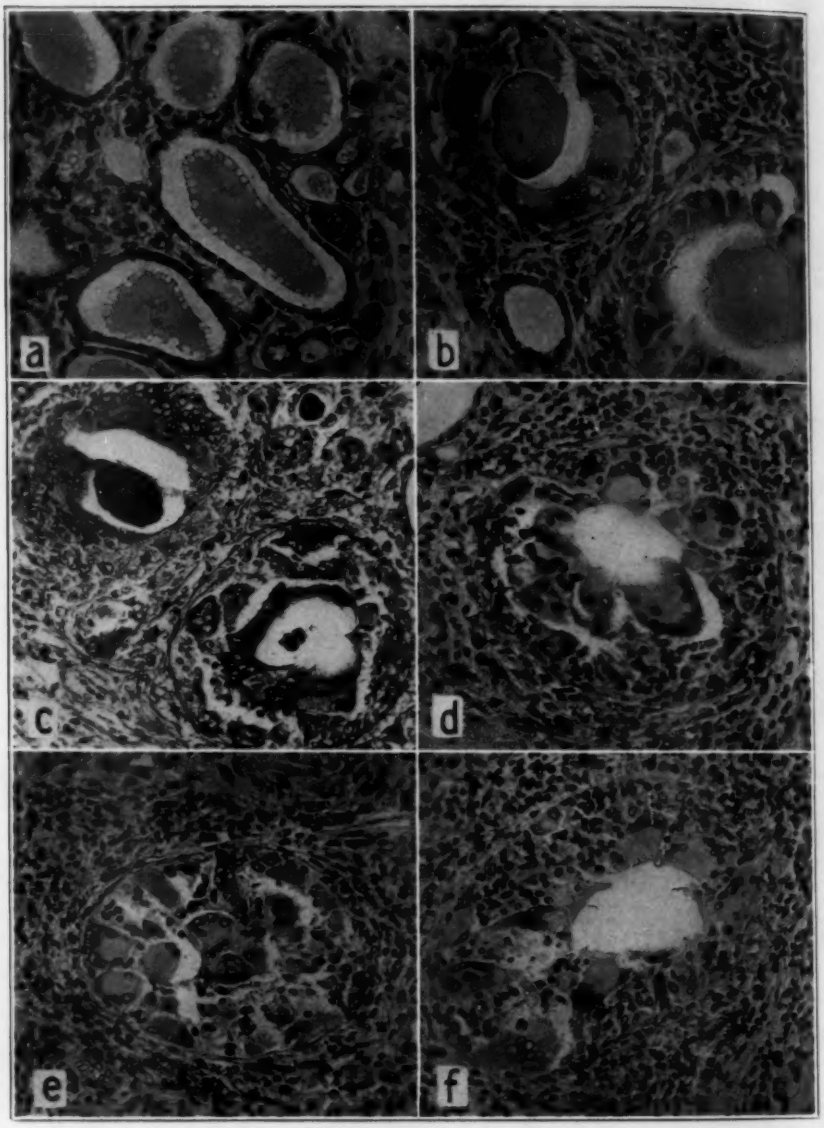

Fig. 4.—Photomicrographs (× 200) illustrating the gradual transitional stages in the life of the giant cells from their origin to virtual disappearance. Note the group of active-appearing follicles (*a*); the early swelling and fusion of adjoining cells with loss of cell definition (*b*); the separation of the fused follicular cells from the basement membrane and their desquamation into the lumens (*c*); the formation of protoplasmic masses with peripherally situated nuclei (*d* and *e*), and the nuclear aggregates in the protoplasmic masses, between which there is an infiltration of undifferentiated connective tissue cells derived from the peri-acinar connective tissue (*f*).

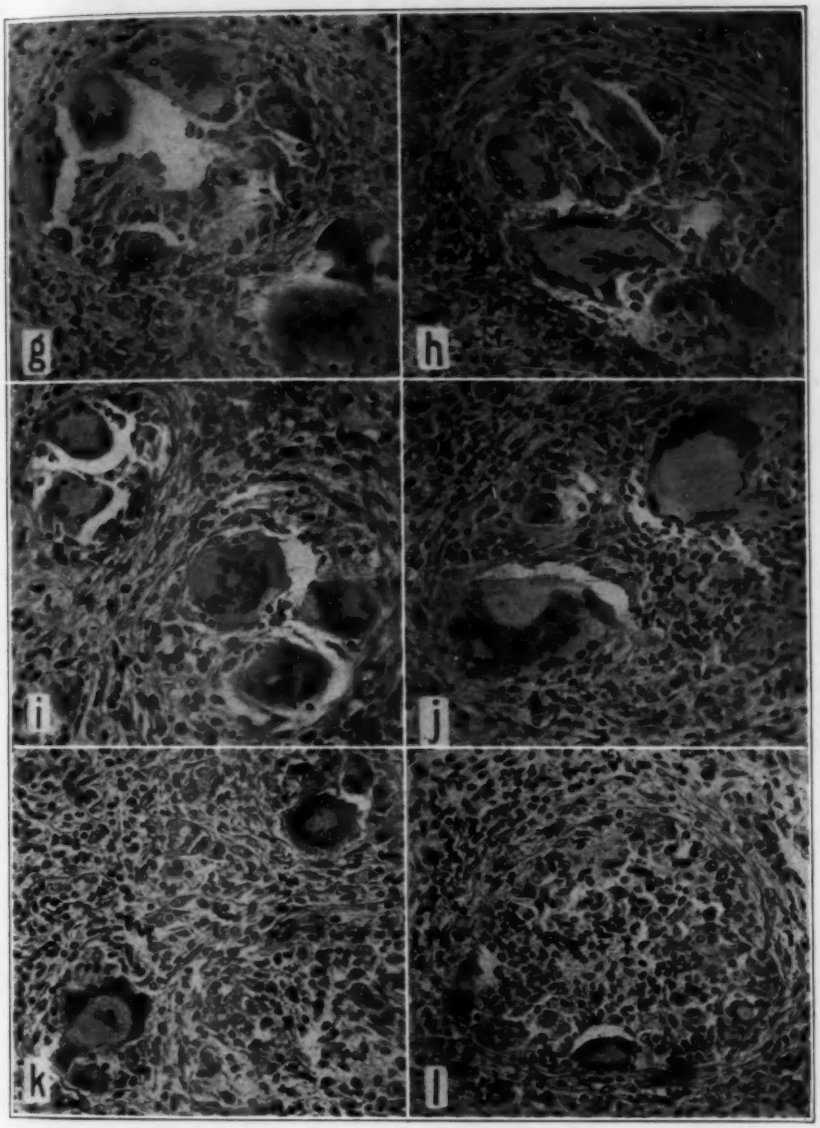

Fig. 5.—Photomicrographs (× 200) showing the more clearly defined, multinucleated protoplasmic masses which assume the appearance of giant cells of various sizes and bizarre shapes (*g* and *h*); shrinkage of follicles and condensation of nuclear aggregates (*i*); crescentic massing of nuclei on one border of the lumen and overlying a mass of protoplasm (*j*); continued degeneration and shrinkage of the giant cells (*k*), and their virtual disappearance in a compact mass of undifferentiated and connective tissue cells and lymphocytes, which fill the follicle (*l*). No evidences of phagocytosis of colloid or cellular debris were seen in any of the aforementioned stages.

nuclei, if recognizable as separate structures, were shriveled, elongated or irregular. They contained little chromatin and showed poor staining affinity for hematoxylin. At this stage remnants of the giant cells at times appeared to lie in the stroma outside the follicles whereas in the previous stages described the giant cells had been definitely within the follicles. Undifferentiated, irregular masses of granular, chromatic material were seen, in which, at times, outlines of nuclei could be recognized. Finally the follicle was completely obliterated by the overgrowth of connective tissue. In none of these later stages were evidences of phagocytosis noted. Moreover, the stages of transition in the formation of the giant cells could be recognized in follicles in which there was no colloid or cellular debris to phagocytose (fig. 5 *g*, *h* and *i*).

COMMENT AND SUMMARY

From this study of follicular degenerative changes which occur in the thyroid gland in the presence of Riedel's struma it is clear that certain conclusions which have been drawn from reported microscopic observations and which concern the occurrence, origin, manner of formation and functional significance of the so-called giant cells are in need of revision. It is essential that one be clear as to the nature of the giant cell in order better to understand the destructive pathologic processes in Riedel's struma. Two conceptions are prevalent; one a fundamental pathologic conception, the second indefinite and confusing. Thus, in one the giant cell is considered a polynucleated, syncytial mass of protoplasm possessed of phagocytic properties and derived possibly from the reticuloendothelial system, or at any rate mesoblastic in origin (MacCallum [13]). In the second conception it seems that any conglomerate, polynucleated mass of protoplasm, regardless of its origin or apparent function, has been designated as a giant cell, and attributes of true giant cells have been assumed. Because of lack of understanding as to the true nature of the giant cells in Riedel's struma, certain previous observers have applied to them the term pseudo giant cells without revealing just what is implied by this term. I have found few reports of microscopic observations dealing to any extent with the so-called giant cells. Often no mention is made of their occurrence. Some authors content themselves with mere mention of their occurrence, while others describe them as foreign body giant cells and assume for them phagocytic properties.

Two views have been expressed as to their origin. Thus Wilke [2] stated the opinion that after desquamation and disappearance of the follicular epithelium the colloid remaining in the acinus acts as a foreign body irritant on the surrounding connective tissue and thus produces an irritative hyperplasia with formation of giant cells which subsequently phagocytose the colloid. A limited number of other writers have suggested that the giant cells probably arise by a process of fusion of the

13. MacCallum, W. G.: Textbook of Pathology, ed. 6, Philadelphia, W. B. Saunders Company, 1937, pp. 156-160.

desquamated follicular cells. As a result of studies reported here I believe that it can be stated that the origin and evolution of the giant cells are invariably anteceded by degenerative and desquamative changes in the follicular epithelial cells, which thereupon lose their cellular identity and fuse with their neighbors to form the commonly observed syncytial, multinucleated masses of protoplasm. As a result of nutritional disturbances and further degeneration the protoplasm of the giant cells becomes scantier, thereby causing the nuclei of these cells to coalesce into conglomerate nuclear aggregates characteristic of the eventual giant cell. It has been possible to trace unquestionable transitional stages in this process. No evidence has appeared to support the view of Wilke; in fact, there are evidences to the contrary, such as the fact that the initial fused protoplasmic masses appeared before the epithelial cells had disappeared and before the lining cells had altogether left their basement membranes and had thus exposed the connective tissue to the irritative action of the colloid. Furthermore, these early stages in the formation of the giant cells were visible in acini entirely devoid of colloid, which had disappeared without the assumed phagocytic action of the giant cells.

The idea that these giant cells arise in response to foreign body irritation of the colloid which they subsequently phagocytose seems in the light of the observations reported here to have been incorrectly assumed by earlier authors and merely to have been accepted and repeated by subsequent investigators. The basis for this assumption has been the reported inclusions in the protoplasm of the giant cells of cellular debris or colloid globules. In the present studies, as also in previously observed cases, no evidences of such inclusions of either foreign material or colloid have been observed.

Since, as has been shown here, the giant cells are derived from coalesced masses of degenerating, desquamated follicular cells which are in the process of destruction for probable nutritional reasons, it seems unwarranted to assume that they have a phagocytic power. If this theory were correct one would be forced to assume that degenerating secretory epithelial cells have acquired the power to engulf and dissolve foreign material, a function reserved for cells originating in the reticuloendothelial system or, at any rate, restricted to mesoblastic tissues. No evidences were found of phagocytic action on the colloid, which could be distinctly differentiated from the protoplasm of the giant cells with such stains as Mallory's connective tissue stain and in the acid fuchsin method for the demonstration of mitochondria (Bensley [12]). Thus, with the former staining method the colloid was bright orange, whereas the giant cell was light violet or purple. This differential staining would readily disclose globules of colloid, if present, in the protoplasm of the giant cells. In rare instances the nuclei were grouped peripherally

about a small central mass of acinar colloid, a fact which could easily be explained by the accidental circumscription of the colloid by the follicular lining cells which had fallen into the lumen. This would further obviate the conclusion that the colloid was engulfed by the giant cell. With the technic for the demonstration of mitochondria it was found that the protoplasm of the fused masses always contained mitochondrial granules similar to those present in the follicular cells before their desquamation, whereas the colloid was always homogeneous and quite devoid of these granulations. Colloid and protoplasm were thus readily distinguishable. No homogeneous colloid bodies were seen in the protoplasm of the giant cells, and it was thus possible to contradict the occurrence of colloid globules undergoing phagocytosis. In the ordinary hematoxylin and eosin preparations confusion might readily arise because of difficulty in differentiating between colloid and the protoplasm of the giant cells due to the similarity in staining reactions and the absence of definitive demonstration of mitochondrial granules.

The giant cells were particularly numerous in the degenerating follicles occurring in the areas of densest fibrosis and consequent greatest nutritional disturbance and were never seen in the more nearly normal-appearing areas of thyroid parenchyma. This fact supports the conception that they are the result of injury followed by desquamation and fusion of follicular cells which are on the road to disintegration. They do not show the viability one would expect from vigorous, newly formed giant cells formed for the purpose of phagocytosis. The fact that they have been assumed to be foreign body cells with phagocytic properties has often rendered difficult the differential diagnosis of Riedel's struma, for their presence has led to erroneous diagnoses, such as tuberculosis, syphilis or even carcinoma, and to consequent incorrect treatment. One is forced, finally, to conclude that the giant cells are structures originally formed by fusion of desquamated follicular cells, which by gradual shrinkage of their protoplasm cause nuclear conglomerates characteristic of the late stage of giant cell formation; that they do not have phagocytic properties and that they are structures of no functional significance but are simply follicular cells on the road to destruction and disappearance in the mass of undifferentiated cells which, in the end, fill and thus obliterate the follicle. If one excludes phagocytosis by the giant cells one will approach more nearly the basic pathologic processes responsible for the destruction of the thyroid parenchyma associated with Riedel's struma.

If by the term giant cells one understands a syncytial, multinucleated mass of protoplasm derived from the reticuloendothelial system and hence mesoblastic and possessed of phagocytic properties, the designation giant cells for the multinucleated masses of protoplasm found in Riedel's struma should be abandoned. The term pseudo giant cell,

implying, as it does, that the structure is not a true giant cell in the sense indicated, might be a more appropriate term. Multinucleated cellular aggregates is a cumbersome term but is more descriptive and is not misleading.

CONCLUSIONS

1. The so-called giant cells associated with the nonspecific thyroiditis designated as Riedel's struma are formed by fusion of follicular epithelial cells into multinucleated, syncytial masses of protoplasm which are desquamated into the lumen of the follicle.

2. These giant cells represent secretory thyroid cells which are on the way to destruction, as is indicated by the readily recognizable transitional stages in their progressive degeneration, final disintegration and eventual disappearance.

3. The observations reported indicate that the protoplasmic giant cell masses seen in Reidel's struma do not possess phagocytic properties as has heretofore been generally assumed and should therefore not be considered true foreign body giant cells.

4. Ultimate understanding of the etiologic factors causing the destruction of the thyroid parenchyma in cases of Riedel's struma will be advanced by realization that the so-called giant cells represent merely a first stage in the disintegration and disappearance of the thyroid epithelium. They are not causes but rather effects of the as yet obscure destructive influences operating in this disease.

ANEURYSM OF THE DUCTUS ARTERIOSUS, WITH A CONSIDERATION OF ITS IMPORTANCE TO THE THORACIC SURGEON

REPORT OF TWO CASES

EVARTS A. GRAHAM, M.D.
ST. LOUIS

The remarkable development of surgery of the chest has greatly increased interest in mediastinal tumors. The removal of such tumors is now a common event. In general it has been my own custom as well as that of others to explore, with the idea of removing them, those which have not responded to roentgen irradiation, unless they are considered to be aneurysms. An unexpected experience in operating on 2 patients with aneurysm of the ductus arteriosus who did not give positive evidence of aneurysm has made me think that the experience should be recorded. This record seems especially desirable because, on the basis of these 2 cases, it would seem as if many of the features are sufficiently characteristic to make one at least suspicious of the presence of an aneurysm of the ductus arteriosus even when no pulsation can be made out. These features will be discussed later.

Although aneurysm of the ductus arteriosus itself is a rare condition, judging from the number of reported cases, it is probable that because of the great interest in thoracic tumors aroused by the modern development in surgery of the chest, thoracic surgeons will encounter the condition much more often than the scanty literature on the subject would indicate. Moreover, in addition to the cases of actual aneurysm of the ductus, there are many more cases in which an unobliterated ductus is associated with an aneurysm of the pulmonary artery. It seems desirable, therefore, that those who are interested in thoracic tumors should be aware of the existence of these aneurysms and of some of their striking characteristics.

Bronson and Sutherland [1] found in the literature up to 1918 only 5 cases of aneurysm of the ductus arteriosus. D'Aunoy and von Haam,[2]

From the Department of Surgery of Washington University and the Barnes Hospital.

1. Bronson, E., and Sutherland, G. A.: Ruptured Aortic Aneurysms in Childhood, with the Report of a Case, Brit. J. Child. Dis. **15**:241, 1918.

2. D'Aunoy, R., and von Haam, E.: Aneurysm of the Pulmonary Artery with Patent Ductus Arteriosus (Botallo's Duct), J. Path. & Bact. **38**:39, 1934.

however, in 1934 were able to collect 18 cases of aneurysm of the pulmonary artery associated with an open ductus arteriosus and they added 2 cases of their own. Costa [3] found that in 46.5 per cent of all patients with aneurysms of the pulmonary artery congenital defects were present and that the most common defect was a persistent ductus arteriosus (20 per cent). Recognition of the possibility of an aneurysm either of the ductus itself or of the pulmonary artery as a complication of a patent ductus not only serves to emphasize the diagnostic confusion which may arise but adds another seldom mentioned argument in favor of surgical closure of recognized patent ductus, especially since Gross and Hubbard [4] have demonstrated the comparative safety of such an operation.

These aneurysms in the majority of cases occur in young adulthood, but they may occur even in advanced age. In Weischer's [5] case the patient was 82 years old and had a saccular aneurysm of the pulmonary artery 15 cm. in circumference, associated with a patent ductus. It is easy to imagine that a vestigial structure like the ductus, which probably has but little tendency to increase in size with the growth of the body, might become stretched out into an aneurysmal sac if exposed for many years to the pressure of the blood in the aorta. It is astonishing that this complication is not more common in cases of patent ductus than it actually seems to be. In the cases of aneurysm of the pulmonary artery associated with a patent ductus the most commonly proposed explanation is that the wall of the artery at the site where the aortic blood strikes it is weakened, becomes sclerosed and then yields to form an aneurysm.

REPORT OF CASES

CASE 1.—A white man aged 31, an engineer for a gas company, was admitted to the Barnes Hospital on Dec. 16, 1936. He had been referred by Dr. James Pittman, of Houston, Texas.

He stated that for the past five or six years he had had a hacking, nonproductive cough and had noticed a slowly increasing dyspnea on exertion. About two weeks previously he had suddenly expectorated about a tablespoonful of liquid dark blood, without cough. On the next two or three mornings he coughed up sputum streaked with small amounts of clotted blood. Roentgen examination at that time revealed a mediastinal tumor. He had noticed for about a year before coming to the Barnes Hospital that he became tired easily, especially after such exercise as swimming or strenuous work.

The previous illnesses consisted of meningitis at 2 years of age; pertussis at 6 years, and operation for hernia and removal of the appendix in 1924. Physical

3. Costa, A., cited by D'Aunoy and von Haam.[2]

4. Gross, R. E., and Hubbard, J. P.: Surgical Ligation of Patent Ductus Arteriosus: Report of First Successful Case, J. A. M. A. **112**:729 (Feb. 25) 1939.

5. Weischer, P., cited by D'Aunoy and von Haam.[2]

examination revealed nothing important or significant except in the thorax. No abnormal heart sounds were detected. Roentgen examination of the chest showed a large rounded shadow, approximately 10 cm. in diameter, projecting to the left of the aortic arch and filling the upper third of the left lung field. The aortic arch was dislocated to the right, as was the trachea. There was a dense ring of calcification which practically surrounded the tumor, which in the lateral view was seen to lie anterior to the spine and close to the anterior wall of the chest. The trachea was dislocated anteriorly by the tumor. The film taken after injection of iodized poppyseed oil showed dislocation of the trachea to the right and displacement of the bronchi of the upper lobe laterally and downward by the tumor, with none of the opaque material overlying the region of the tumor. The films of the spine showed no evidence of a destructive process involving the bony cage. The roentgen diagnosis was mediastinal tumor (dermoid cyst) with cardiac and tracheal dislocation, although it was recognized that the location of the tumor, posterior to the trachea, was unusual for a dermoid cyst.

The electrocardiogram was normal. Fluoroscopic examination showed no pulsation of the mass. Examination of the blood and of the urine revealed no abnormality. The Wassermann and Kahn reactions were negative, as was the result of a fixation test for echinococcus disease.

On December 19, with intratracheal cyclopropane anesthesia, the patient was operated on. An anterior incision in the fourth left interspace was made. The second, third, fourth and fifth costal cartilages were divided, and the pleura was entered. The upper part of the left lung was found to be rather firmly adherent to the tumor but was separated from it by dissection with the finger. The tumor itself felt very firm. It presented on its left lateral aspect an area about the size of a half-dollar which was slightly yellow and calcified. No sign of fluctuation was elicited in the tumor, and it seemed, therefore, to be semisolid rather than cystic. It was so firmly attached to the surrounding structures that it was immobile. The mediastinal pleura was dissected free from the mass on the left, but no satisfactory mobilization of the tumor could be made. Certain anatomic abnormalities were noted, such as an unrecognizable aorta. The impression was received that perhaps the tumor was a malignant teratoma which had invaded the surrounding tissues. It seemed, however, that perhaps some relief of pressure might be obtained by opening the tumor and removing its contents. Accordingly, an incision about ½ inch (1.2 cm.) long was made in its left anterior lateral aspect. Yellowish putty-like contents bulged out of this incision. Suddenly a swishing sound was heard, caused by a terrific hemorrhage from the tumor, which was like a blow-out. An attempt was made to arrest the hemorrhage by pressure, but the tissue was so friable that the tumor was torn, and the hemorrhage could not be arrested by that method. The patient's blood pressure rapidly dropped to a point where it could not be recorded, and the heart practically stopped beating. Blood was available in the operating room, and fluid was already going into a vein in the foot. A blood transfusion was, therefore, started immediately, and 1 cc. of epinephrine hydrochloride was injected into the muscle of both the right and the left ventricle. Moreover, massage of the heart was started, and in about two minutes it began to beat more forcibly. During the time that the blood pressure was very low the hemorrhage from the tumor had practically ceased. A hasty exploration with the finger revealed that there was almost certainly an aneurysm. Mattress sutures of no. 2 chromic catgut were passed rapidly through

the tumor in an effort to control the hemorrhage. This was successful, and as a result of the transfusion of 500 cc. of blood together with 500 cc. of dextrose and acacia the patient's blood pressure returned to 170. It seemed that his condition was entirely satisfactory, and the wound in the chest wall was being closed in the usual way, when suddenly his respiration ceased, and within about one minute his heart stopped beating. Efforts to revive him again by the same methods were this time unsuccessful, although there had been no hemorrhage in the meantime. It was suspected that the patient probably had emboli to the respiratory and cardiac centers. Death occurred on the table.

The anatomic diagnoses at autopsy were as follows: (1) right aortic arch with the left subclavian artery as the last main vessel coming from the arch; (2) aneurysm of the partially obliterated ductus arteriosus; (3) recent thoracotomy wound on the left, with incision and suture of the wall of the aneurysm; (4) left

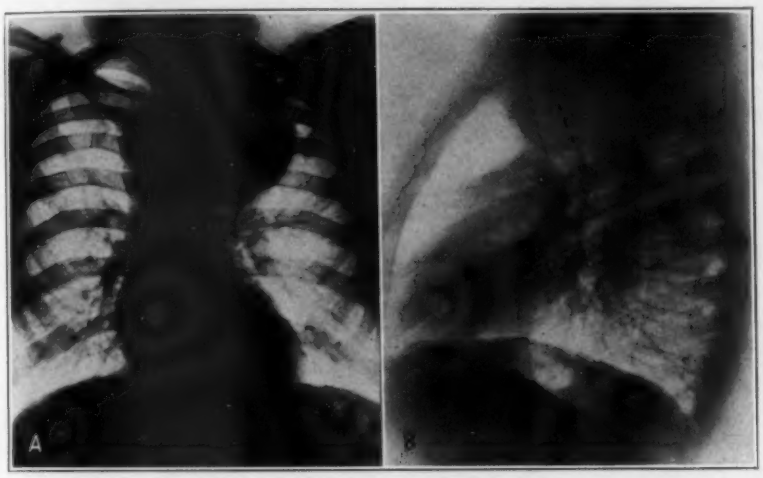

Fig. 1 (case 1).—*A*, anteroposterior film. The calcified periphery of the aneurysm is plainly seen. *B*, lateral view, slightly retouched to show the position of the trachea in relation to the aneurysm.

hemothorax; (5) collapse of the left lung; (6) embolus in the right vertebral artery adjacent to its junction with the left artery; (7) multiple small hemorrhages in the myocardium; (8) moderate hypertrophy of the left ventricle; (9) pulmonary edema; (10) patent foramen ovale; (11) old right inguinal operative scar.

Pathologic Examination.—A large tumor was observed occupying the apex of the left pleural cavity, pressing into the root of the neck and compressing the upper lobe of the left lung downward and backward. Medially the tumor pressed against the trachea and caused it to deviate slightly to the right. Instead of passing anterior to the trachea and dipping down behind the left bronchus, the aorta passed to the right and behind the trachea and esophagus and then followed its normal course along the vertebral column. It was also noted that the first main artery to come off the arch was the left internal carotid. After removal of the thoracic organs it was seen that the large tumor was attached to the

arch at the level at which it became continuous with the thoracic aorta. The tumor was roughly spherical, with indentations at points where resistance had been encountered. Three diameters were measured and were recorded as 11, 8 and 7.5 cm., respectively. The tumor had a somewhat rubbery, elastic feel and a covering which was formed of a thin plate of irregularly calcified tissue. Posteriorly and medially the tumor had rested on the bodies of the upper thoracic vertebrae, and here it showed a slight indentation. The bodies of the thoracic vertebrae had been noticeably eroded by the pressure of the tumor.

The aorta was opened along its lesser curvature, and there was a circular opening 2 cm. in diameter which communicated directly with the tumor mass.

Fig. 2 (case 1).—Photograph of the autopsy specimen. The large mass above the left lung and next to the trachea is the aneurysm. The abnormal position of the aorta on the right side is clearly seen. For evidence that the aneurysm involved the ductus arteriosus, see the text.

This opening had rounded, smooth margins covered with endothelium but quickly passed into a large cavity filled with an old laminated, partially broken-up blood clot. The opening lay just below the exit of the left subclavian artery from the arch. The subclavian artery coursed up along the anterior surface of the tumor to enter the root of the neck, but, although it was closely adherent to the tumor, it did not communicate with it. The intimate connection to and direct communication with the aorta plus the character of the tumor wall and its contents clearly indicated that this was an aneurysm. An attempt was made to determine the origin of the aneurysm.

The aorta arose in the normal manner from the left ventricle, but the arch was formed chiefly by the right arch instead of the left arch. The left arch had disappeared except for the very small segment to which the left subclavian artery was attached (fig. 2). The right arch, which normally drops out in embryonic life, was retained in its entirety. The left common carotid, right common carotid and right subclavian arteries arose in that order from the right aortic arch. The pulmonary artery left the right ventricle in the normal manner and divided into the right and the left pulmonary artery. On the anterior superior surface of the proximal portion of the left pulmonary artery was the small, partially obliterated stump of the ductus arteriosus. This stump had been severed either at operation or at autopsy and appeared as a short fibrous cord arising from the wall of the pulmonary artery. However, if the tumor was placed in the position it had originally occupied the fibrous cord was shown to lie adjacent to a small sacculation arising from the tumor. At the apex of this small sacculation there was a

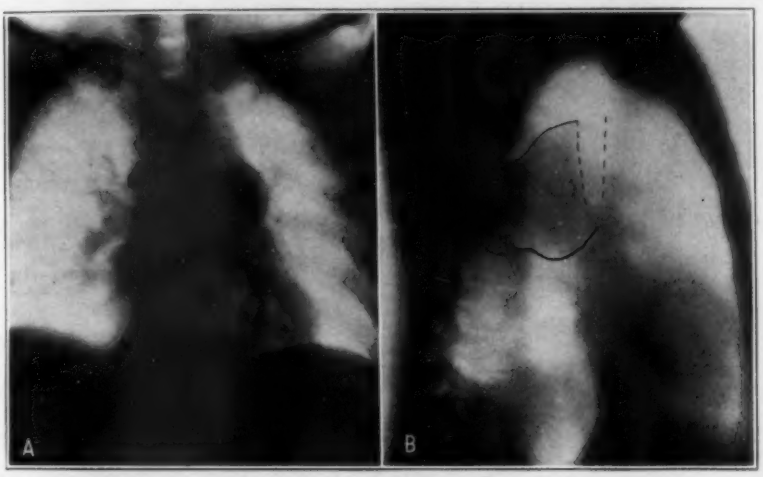

Fig. 3 (case 2).—*A*, anteroposterior laminogram. *B*, lateral laminogram. The aneurysm and the trachea have been retouched to show more plainly the position of the aneurysm as posterior to the trachea.

fibrous nodule which corresponded to the fibrous cord arising from the pulmonary artery. The apex of the sacculation was cut off, and a short tube was observed, about 5 mm. in diameter, leading directly into the aneurysm. From these observations the conclusion was reached that the aneurysm involved the ductus arteriosus. The pulmonary arterial end of the ductus was obliterated and was represented merely by a fibrous cord. However, this fibrous cord shortly opened up into a definite tube, which was about 1 cm. long and which entered a large saccular aneurysm. This aneurysmal sac in turn communicated with the arch of the aorta just below the exit of the left subclavian artery and in the region where the ductus arteriosus had communicated with the aorta in fetal life. The conclusion, then, that this was an aneurysm of the ductus arteriosus was inescapable.

The heart was of normal size and none of the chambers appeared dilated or hypertrophied. The foramen ovale was open, but a septum was present which

practically covered the opening. There was no patent intraventricular septum, but the septum was very thin. In the left ventricular myocardium there were several small areas which were hemorrhagic and had a soft feel. No blocks were observed in the larger divisions of the coronary vessels, but it was thought that these areas might represent early infarction caused by emboli in the small branches of the artery. The coronary vessels showed no sclerosis. There were no lesions of the endocardium or of the valve cusps.

CASE 2.—A white man aged 27, a miner, was admitted to the Barnes Hospital June 12, 1939. The chief complaints were wheezing spells, shortness of breath

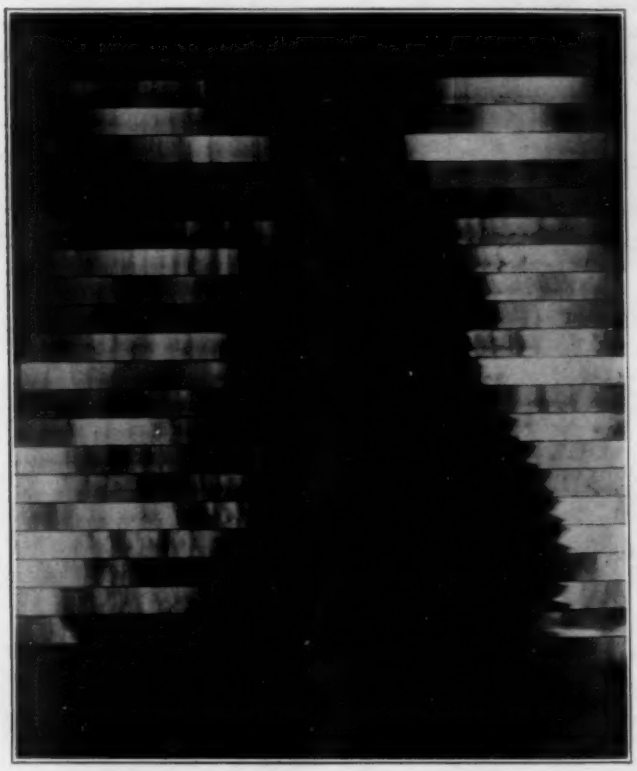

Fig. 4.—Roentgenkymogram which was interpreted as not showing the expansile pulsation of the tumor.

on exertion and cough following exertion. He was inclined to date all his trouble from an automobile accident seven years ago, as a result of which he lost several teeth, bruised his knees and received a blow on the chest. He was not told, however, that any ribs were fractured as a result of the accident. About two months later his mother noticed that he wheezed after exertion. This had gradually increased to such an extent that he was not able to work or to do anything which required exertion. Occasionally he had a strangling sensation. Otherwise he had no complaint, and his general appearance was that of a normal young man.

Examination.—The only significant features revealed by the examination were those concerned with the thorax, particularly the roentgen picture. The patient was examined with ordinary films, with Potter-Bucky films, with roentgenkymograms and finally with laminograms (figs. 3 and 4). Overlying the upper border of the heart at the level of the pulmonary conus was a rounded, pedunculated mediastinal tumor which lay anterior to the spine and posterior to the trachea. The pedunculation of the tumor seemed particularly evident in the lateral laminogram, and the pedicle seemed to be attached to an intervertebral arch. The heart was within normal limits. The pulsation which was noted in the tumor was considered on the basis of the roentgenkymogram to be transmitted rather than expansile. No abnormal heart sounds were heard. The diagnosis from the electrocardiograms was sinus bradycardia with auricular premature beat. The pulse rate was 70. The blood pressure was 133 systolic and 83 diastolic. The blood count, urinalyses and determinations of the values for blood sugar and urea nitrogen revealed no abnormality. The Kahn reaction was negative. The vital capacity was 4,350 cc.

Because of the apparent pedicle of the tumor and the fact that no expansile pulsation was seen it was felt that the most probable diagnosis was tumor of the posterior part of the mediastinum, perhaps neurofibroma.

At operation on June 15, a posterior thoracotomy was made by elevating the scapula and dividing the posterior portions of the fourth, fifth and sixth ribs. In the arch of the aorta a tumor about the size of an orange was seen, filling the entire concavity of the arch of the aorta. The tumor was clearly wedged in between the aorta and the pulmonary artery. The mass seemed to pulsate synchronously with the aorta. It was felt, therefore, that it must be an aneurysm. In order to prove the diagnosis a small needle on a hypodermic syringe was inserted into the mass, and arterial blood was withdrawn readily through the needle. Because the aneurysm was in the anatomic location of the ductus arteriosus and because of the similarity of this case to case 1 it was felt that the aneurysm was one of the ductus arteriosus. For fear of rupturing the sac no further dissection was carried out, and the thoracotomy wound was closed without drainage.

The patient recovered satisfactorily from the operation. Information received from him seven months later stated that his symptoms were about the same as before the operation.

Comment.—It is realized, of course, that positive proof that the aneurysm in this case originated in the ductus arteriosus is lacking without the demonstration of an opening of the ductus into the sac. On the other hand, the diagnosis seems to be the most probable one. The question as to whether the automobile injury seven years previously had anything to do with creation of the aneurysm seems to me relatively inconsequential. If the patient had a patent ductus arteriosus at the time of the injury it is not unlikely, perhaps, that trauma to the wall of the ductus might have hastened the development of the aneurysm. On the other hand, it would seem unlikely that so insignificant a trauma as one which failed to fracture any ribs would have resulted in a sufficient injury to the aorta itself to cause an aneurysm of the arch.

GENERAL COMMENT

In retrospect, on the basis of these 2 cases it would seem that certain common findings stand out as features which would strongly suggest the possibility of an aneurysm of the ductus arteriosus. The most important diagnostic feature is the location of the tumor in the superior mediastinum, in the region of the pulmonary conus and lying posterior to the trachea. On the other hand, the more common varieties of mediastinal

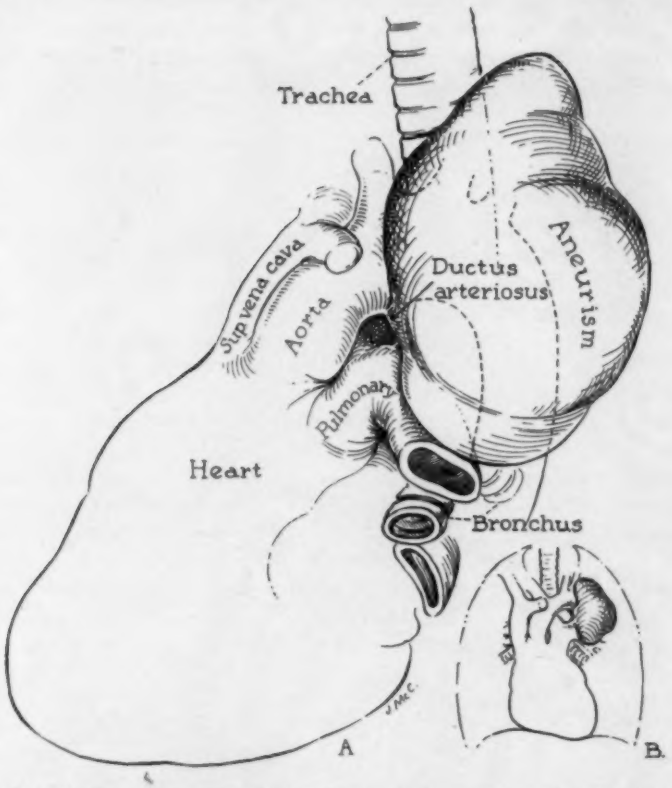

Fig. 5.—Diagram reconstructed in case 2 to show the mechanism of position of aneurysms of the ductus arteriosus posterior to the trachea. The large drawing is a lateral view. The inset is an anteroposterior view. An aneurysm of the ductus pushes itself out between the pulmonary artery and the aorta to assume a left lateral and posterior position.

tumor are seldom found in this location. Dermoids and teratomas are usually tumors of the anterior mediastinum; likewise, although thymic tumors and those which arise in the lymph glands (lymphosarcoma and Hodgkin's disease) are most often found in the superior mediastinum, they are not located so nearly in the region of the pulmonary conus as

are aneurysms of the ductus arteriosus. On the basis of probability, therefore, a tumor posterior to the trachea in the region of the pulmonary conus should be suspected of being an aneurysm of the ductus arteriosus or of the pulmonary artery (fig. 5). Absence of recognizable expansile pulsation even in roentgenkymograms and of abnormal heart sounds is of no significance, as the 2 cases reported here illustrate. It was astonishing to me that neither patient gave evidence of a disturbance of the left recurrent laryngeal nerve. Moreover, I do not find this complication mentioned in the literature. Probably in most cases an exploratory thoracotomy is advisable. It may perhaps be predicted that some day an aneurysm of the ductus arteriosus will be found small enough to permit excision.

STERILIZATION OF THE AIR IN THE OPERATING ROOM WITH BACTERICIDAL RADIATION

RESULTS FROM NOV. 1, 1938 TO NOV. 1, 1939, WITH A FURTHER REPORT AS TO SAFETY OF PATIENTS AND PERSONNEL

DERYL HART, M.D.

DURHAM, N. C.

As interest in the use of ultraviolet rays of certain wavelengths as an agent for killing micro-organisms in the air, particularly in the operating room, has become more widespread, the questions most frequently asked have concerned the results obtained by its use and the possible danger to the patient and to the operating room personnel. Since probably I have had the greatest experience with this recent addition to surgical technic as a routine in all large clean operative procedures, a further report of my experience and results may be of interest and value in this field.

The first operation on a patient in the Duke Hospital in a field of ultraviolet radiation was performed on Jan. 15, 1936. A preliminary report [1] based on several years' study of viable bacteria in the air, showing how they can be reduced by air conditioning and almost eliminated by radiation, was made after experience with 9 thoracoplasties had demonstrated great improvement in the local and systemic reaction of the patient. This was not published, however, until May 1937. Subsequently, in May 1936, a paper based on this preliminary work and on experience with 18 extrapleural thoracoplasties was read before the American Association for Thoracic Surgery and was published in October.[2] The operations on patients had been preceded by experimental studies on bacteria [3] and on wound healing in animals,[4] beginning

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From the Department of Surgery, Duke University School of Medicine and Hospital.

1. Hart, D.: Operation Room Infections: Control of Air-Borne Pathogenic Organisms, with Particular Reference to the Use of Special Bactericidal Radiant Energy; Preliminary Report, Arch. Surg. **34**:874-896 (May) 1937.

2. Hart, D.: Sterilization of the Air in the Operating Room by Special Bactericidal Radiant Energy, J. Thoracic Surg. **6**:45-81 (Oct.) 1936.

3. Hart, D.; Devine, J. W., and Martin, D. W.: Bactericidal and Fungicidal Effect of Ultraviolet Radiation: Use of a Special Unit for Sterilizing the Air in the Operating Room, Arch. Surg. **38**:806-815 (May) 1939.

4. Hart, D., and Sanger, P. W.: Effect on Wound Healing of Bactericidal Ultraviolet Radiation from a Special Unit: Experimental Study, Arch. Surg. **38**:797-805 (May) 1939.

in the fall of 1934. The application of this technic to operations on patients was delayed, since it required approximately a year to interest a manufacturer in the project, and then the equipment had to be assembled and installed.[5]

From the opening of the Duke Hospital, in July 1930, until Jan. 15, 1936, a total of 15,557 operations were performed, with 7 known deaths[6] resulting from infection in clean operative wounds (extrapleural thoracoplasty, 4; craniotomy, 2; radical mastectomy, 1). From Jan. 15, 1936 to Nov. 1, 1939, all thoracoplasties, mastectomies and repairs of postoperative ventral hernias and most other large clean operations in the general surgical service have been performed in a field of ultraviolet radiation. For the past two and one-half to three years practically all large clean operative procedures in the neurosurgical, orthopedic and urologic services have also been performed in such a field. During these three years and nine and one-half months, of a total of 23,216 operations approximately 2,000 were clean operations performed in a field of bactericidal radiation. No patient operated on in this group, which includes most of the larger procedures, has died as a result of an operative wound infection.[7]

The results up to the fall of 1937, showing a reduction of over 75 per cent in all infections in clean operative incisions, have been reported. There were only two questionable operating room infections.[8] (1) a stitch abscess and (2) a separation of the edges of the skin due to inversion of the skin, with a "positive" culture of material from the granulating area, in 364 clean primary incisions in the general and orthopedic surgical services when radiation was used. The infection rate for operations of an average magnitude less than that for these 364 operations was 3.5 per cent in 144 orthopedic and 3.6 per cent in 536 general surgical operations.

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5. The Westinghouse Electric and Manufacturing Company have supplied all radiation equipment.

6. There were probably other deaths from operating room infections in clean wounds in the other surgical services. A complete analysis is being made and will be published.

7. During this period 1 patient, on whom a craniotomy was performed without bactericidal radiation for an inoperable glioma when the only room equipped for radiation was in use for a laminectomy, died of meningitis (hemolytic Staphylococcus aureus). This was the only death during this period from an operating room infection in a clean incision in the general, thoracic and neurologic surgical services. All the 23,216 records have not been reviewed, and there may have been some deaths from operating room infections in other services, in which radiation was not used. These are being reviewed, and the results will be published.

8. Hart, D.: Sterilization of the Air in the Operating Room by Bactericidal Radiant Energy: Results in Over Eight Hundred Operations, Arch. Surg. **37**:956-972 (Dec.) 1938.

The considerable reduction in the average duration and elevation of postoperative temperature reaction for thoracoplasties, mastectomies and herniorrhaphies brought about by sterilization of the air has been reported.[9] These results were correlated with the seasonal fluctuations in the contamination of air, showing that the reduction in temperature reaction was directly proportional to the diminution in the degree of contamination of air.

TABLE 1.—*Operations at the Duke Hospital from Nov. 1, 1938 to Nov. 1, 1939*

		Postoperative Infections Diagnosed on Discharge of Patient		Postoperative Infections Found on Review of Records *	
	Total	Number	Percentage	Number	Percentage
Total number of operations.....	6,535 [a]	23 [b]	0.35 [c]	Records not reviewed	
Clean primary incisions with bactericidal radiation	606	2 [d]	0.33	4 [e]	0.66
Total number of potentially infected or reopened wounds with bactericidal radiation	88	5 [f]	5.7	19 [f]	21.8

* All these were related to the original disease or were either slight or questionable.

a. All operations, including drainage of infected areas, operations on the nose and throat, transurethral prostatic resections, etc., are included.

b. Under the rigid criteria which my associates and I use for healing without infection in the group in which radiation was used there were undoubtedly more than 23 infections, but the postoperative wound infections not diagnosed in the record have in general been slight or related to the preexisting disease. On previous occasions a careful analysis of records when radiation was not used has shown an infection rate of 3.5 per cent to 4 per cent for clean primary incisons exclusive of thoracoplasties.

c. This percentage is low, since slight infections and infections related to the preexisting disease may not have been diagnosed, while the total number of operations includes the drainage of infections, operations on the nose and throat, transurethral prostatic resections, etc.

d. One of these was an infection in an incision made through abraded skin and contused muscle for a fracture-dislocation of the spine and was probably hematogenous (see abstract and temperature chart 3). The other was an infection following an arthroplasty of the hip; the wound was drained, and a postoperative hemorrhage occurred (see abstract and temperature chart 4).

e. These infections (cases 1, 2, 5 and 6 [see abstracts and charts]) were slight, superficial, doubtful or due to a fault in technic. A brief abstract and postoperative temperature chart of each is given.

f. See tables 3 and 4 for an analysis of these infections.

RESULTS OBTAINED

The first point of interest, the recent postoperative results obtained with bactericidal radiation, is illustrated by an analysis of the operations performed from Nov. 1, 1938 to Nov. 1, 1939. Table 1 shows that of a total of 6,535 operations bactericidal radiation was used throughout 606 clean primary incisions and 88 other operations in which the wounds were potentially infected or which involved reopening of a recent incision. Only 2 of the 606 clean primary incisions were diagnosed as showing postoperative wound infection at the time of the patient's dis-

9. Hart, D., and Upchurch, S. E.: Postoperative Temperature Reactions: Reductions Obtained by Sterilizing the Air with Bactericidal Radiant Energy; Seasonal Variations, Ann. Surg. **110**:291-306 (Aug.) 1939.

charge. One of the operations was a laminectomy in which I consider the infection to have been hematogenous even though the operation for a fracture of the spine of ten hours' duration was performed through abraded skin and contused muscles which were infiltrated with blood

TABLE 2.—*Operations Performed With Bactericidal Radiation from Nov. 1, 1938 to Nov. 1, 1939 (Clean Primary Incision)*

Type of Operation	Without Postoperative Infection	With Postoperative Infection	Comment
Thyroidectomy, 63; laparotomy, 23; thoracotomy, 2; miscellaneous, 67; lumbar incisions, 8	163	0	
Operations on breast: radical, 28; simple, 9; excision of benign tumor, 11	48 [a]	0	
Amputation, 8; operation for bone tumors, 23; open reduction of fractures, 17; spinal fusion, 11	59	0	
Operation for hernia: inguinal, 80; femoral, 4; umbilical, 2; postoperative ventral, 10	95	1 [b]	Stitch abscess; maximum temperature, 37.6 C.
Craniotomy	90 [c]	1 [d]	Stitch abscess; incision in scar; spinal fluid drainage
Laminectomy (including meningocele repair)	57	1 [*e]	Abrasion and contusion of skin; infection (hematogenous ?)
Opening of joints	35	2	In 1, drainage and hemorrhage [*f]; in 1, necrosis of skin [g]
Extrapleural thoracoplasty	16 [h]	1 [i]	
Plastic procedures	37 [j]	0	
Total	600	6	

* Diagnosed on the patient's discharge from the hospital. Other infections were slight, questionable or related to the primary disease and were found on careful review of the records.

a. Four of these were associated with some necrosis of the skin (without evident infection) resulting from a poor blood supply due to close cutting of the skin flaps.

b. See abstract and temperature chart 1.

c. Two of these followed roentgen treatment, and one, without such treatment, showed small areas of cutaneous necrosis, while two of them had cerebrospinal fluid drainage. All, however, were without evidence of infection.

d. See abstract and temperature chart 2.

e. See abstract and temperature chart 3.

f. See abstract and temperature chart 4.

g. See abstract and temperature chart 5.

h. See abstract and temperature chart 7. In 1 of these cases, in which there was a normal temperature after the third postoperative day, organisms were cultured from a pocket of fluid in the wound (grossly not infected) at the time of the second operation.

i. See abstract and temperature chart 6.

j. After certain of these operations performed in multiple stages there may have been a "positive" culture of material from a granulating area where the skin could not be closed, but none of the wounds showed suppuration or interference with the operative procedures.

(case 3). The other was an arthroplasty of the hip in which a drain was inserted and the patient had a postoperative hemorrhage. The infection was first noted on the ninth day following operation and was considered to be superficial, resulting from the open drainage tract and the hematoma in the wound (case 4). Four other infections, mostly slight or questionable, were picked up on careful review of the 606 records. The classification of these operations is given in table 2. In

order to present as complete and as accurate a picture as possible, every infection, however questionable, is included, even though I may feel that it occurred as a result of the technic used (case 5 and possibly case 4) or that the infection was not received in the operating room (stitch abscesses, cases 1 and 2). There are presented a brief abstract of each case record and the temperature chart for seven days after operation in each case of a clean incision which has been included as possibly infected. Each reader can, then, make his own interpretation as to whether there was an infection originating in the operating room. The infection rate of 1 per cent, as shown in table 2, can therefore be lowered by individual interpretation of these abstracts but not raised.

Data on the reopened wounds are given in table 3. Of the 2 thoracoplasty incisions noted as infected, 1 had shown an infection following the

TABLE 3.—*Operations Performed With Bactericidal Radiation from Nov. 1, 1938 to Nov. 1, 1939 (Reopened Wounds—Second Stage Operations)*

	Without Postoperative Infection	With Postoperative Infection
Extrapleural thoracoplasty....	5	2 (1 with infection in first stage [a]; 1 with organisms in wound [b] at operation)
Thyroidectomy (2d lobe).....	10	0
Laminectomy.....	1	0
Postoperative ventral hernia..	1 [c]	0
Total.....	17	2

a. See abstract and temperature chart 6. This infection was diagnosed on discharge of the patient from the hospital. There was an undiagnosed infection (considered by the operator as only a draining hematoma) following the first operation; a granulating area was excised at the time of the second operation, and cultures of material taken from deep in the wound at this time showed viable hemolytic yellow staphylococci to be persistent.

b. See abstract and temperature chart 7. The hemolytic Staph. aureus was cultured from a pocket of fluid beneath the scapula at the time of the second operation. This infection with the same organism following the second operation was slight, the organisms being cultured from a draining hematoma, and the drainage never became purulent.

c. Infection was suspected; the wound was explored in the operating room; no pus was found; cultures were sterile; the wound was reclosed without drainage, and primary healing resulted.

first stage; a granulating area was excised in making the incision for the second stage, and viable organisms were present deep in the wound. The other showed a positive growth of organisms from a pocket of fluid beneath the scapula at the second operation. Both infections were mild. (See abstracts and temperature charts 6 and 7 for both first and second stages.) These 2 infections in the reopened wounds were evidently continuations of the condition originating from entrance of the organisms at the time of the first operation. I still believe that viable organisms enter every wound, but with radiation these are greatly reduced, and the survivors may be attenuated. The rate of infection in these thoracoplasty incisions is out of all proportion to the rate of infection in a

TABLE 4.—*Operations Performed With Bactericidal Radiation from Nov. 1, 1938 to Nov. 1, 1939 (Infected or Potentially Infected Incisions)*

Type of Operation	Without Postoperative Infection	With Postoperative Infection	Comment
On colon, 5; on stomach and intestine, 6; on appendix, 5; on gallbladder, 5	19 [a]	3 (1 colon*)	
Lobectomy and pneumonectomy	7 [b]	0	
Hernia: Inguinal	0	1 [c *]	Local dermatitis
Femoral	0	1 [d]	Gangrenous intestine
Pylephlebitis; drainage of splenic abscess	0	1 [e]	
Secondary closure	0	1 [f]	Infection around tension sutures
Excision of ulcer; skin graft	1	2	
Operations on kidney and on ureter	20	6 [g]	Drainage in all; infected urine in all; 4 very slight infections; no severe infections
Meningocele repair (abscess opened during operation)	0	1	
Craniotomy (lacerated scalp—infected)	0	1	
Craniotomy (for subdural and extradural hemorrhage)	0	1 [h]	Followed wound rupture with sinus formation; two preceding aspirations; cultures sterile
Bone graft (for old osteomyelitis)	0	1 [*]	
Opening joints; anthroplasty of hip; infection and abrasions of skin	0	1 [*i]	
Removal of cartilage from knee; infection of skin	0	1 [j]	Organisms cultured from joint at operation; W.B.C., 10,200 per cu. mm.; mild or doubtful
Old pyarthrosis of wrist; scar; unable to close	0	1	
Total	47	22	

* Diagnosed on the patient's discharge from the hospital. Other infections were slight, questionable or related to the primary disease and found on review of the records.

a. In some of these cases there may have been a "positive" culture of material from the drainage tract, but there was no gross suppuration and no drainage from other parts of the wound.

b. In 3 of these cases the wound was drained. Cultures showed no growth after operation, but they yielded bacteria after a more or less prolonged period of drainage.

c. This operation should not have been performed, since a note the day before operation described a dermatitis in the operative region.

d. Resection of gangrenous intestine.

e. Exploratory laparotomy. A splenic abscess secondary to pylephlebitis resulting from undiagnosed appendicitis was found and drained.

f. Only the reaction about cutting tension sutures of wire inserted for secondary closure of a disrupted laparotomy incision.

g. Most of these showed nothing more than slight infection when the drains had been left in for several days.

h. The hematoma reformed. It was aspirated twice, and the cultures were sterile. A culture yielding bacteria was obtained only after rupture through the incision had occurred, with formation of a draining sinus.

i. The patient was admitted from the dispensary wtih a note that admission was advised for the purpose of treating the cutaneous condition (furuncles and abrasions on the leg) on which the arthroplasty was to be performed. Two days later, for some reason not explained, an arthroplasty was performed. Evidently this operation should have been postponed.

j. The patient showed furuncles on the leg and a leukocyte count of 10,200 per cubic millimeter before operation. The hemolytic Staph. aureus was cultured from the fluid in the joint when it was opened. On the fourth day, after the culture of material taken at operation was reported as yielding bacteria, the wound was opened superficially, and a note was made that it was infected, but cultures of material taken at this time were sterile. On the ninth postoperative day the suprapatellar bursa was irrigated, and cultures showed no growth. On the eleventh postoperative day material from the superficial tissues of the wound showed Bacillus alcaligenes faecalis. Twenty-nine days later the wound was healed, and the knee had the full range of motion.

larger series of thoracoplasties previously reported as performed with the aid of radiation.[10]

Table 4 records the potentially infected operative wounds and is of little significance here except as it illustrates some of the operations performed with bactericidal radiation and includes all operations with radiation not given in tables 2 and 3.

Table 5 shows data on all other postoperative infections (operations performed without bactericidal radiation) diagnosed at the time of the patient's discharge. It is seen that all these infections except those in the obstetric and gynecologic services were directly related to the primary disease. There were undoubtedly other mild infections or infections related to the primary disease in the cases in which radiation was not

TABLE 5.—*Operations Performed Without Bactericidal Radiation from Nov. 1, 1938 to Nov. 1, 1939 (All Postoperative Infections Diagnosed on Discharge of Patient)*

Operation for	Total Number of Postoperatively Infected Wounds *	
Acute appendicitis	5	
Acute cholecystitis	3	
Intestinal obstruction	1	
Perforated duodenal ulcer	1	
Cesarean section	2	Obstetric and Gynecologic Service [a]
Hysterotomy, 1; hysterectomy, 1	2	
Perineal laceration	2	

* Only infections diagnosed at the time of the patient's discharge. The several thousand records of wounds not diagnosed as showing infection were not reviewed as was done for the operations performed with use of radiation.

a. Six of these were in the obstetric and gynecologic service, in which radiation is not used. The others were all related to the primary disease. All large clean operations in the general, urologic, orthopedic and neurologic surgical services were performed in a field of bactericidal radiation, and data on them are shown in tables 2, 3 and 4. This table is included to show the types of operation in which radiation was not used as well as to report all diagnosed wound infections occurring when radiation was not used.

used, but it can be safely assumed that there were no *serious* infections in clean wounds, since these are included in the diagnosis file. Review of these several thousand records of operations performed without use of radiation for mild infections, such as stitch abscesses, did not seem indicated for this report. This table is given to show all diagnosed postoperative infections occurring when radiation was not used and indicates that all large clean operations except those in the obstetric and gynecologic service were performed in a field of ultraviolet rays.

SAFETY OF THE PATIENT

The second point of interest, the safety of the patient, is best proved by the fact that with an intensity of radiation on the wound varying

10. Hart, D.: Sterilization of the Air in the Operating Room with Bactericidal Radiation, J. Thoracic Surg. **7**:525-535 (June) 1938.

from 25 to 34 microwatts per square centimeter with different installations,[11] without any allowance for shading by the personnel, my associates and I have performed over 2,000 operations (general, thoracic, plastic, orthopedic, urologic and neurologic procedures), the majority lasting for from one to several hours, and have never seen any ill effects on, or had any complaint from, any patient referable to the radiation. Before this radiation was used on patients, many experiments were made on bacteria[3] to determine its killing effect, and many operations were performed on rats and on dogs[4] to determine the possibility of its damaging the tissues. During the earlier operations an assistant was assigned the duty of seeing that every part of the wound was covered when exposure was not absolutely necessary for the operative procedure. It was soon learned that this precaution was not necessary, so that now the tissues are covered with moist cloths or cotton, as determined by good surgical technic, but this duty is not assigned to an overzealous assistant instructed to protect them from the radiation even at the expense of the surgeon's efficiency.

Criticism of the intensity of radiation used by my associates and me was made in a recent article[12] stating that this is greater than is necessary to reduce the organisms in the air, that it may be in the danger zone for tissue injury and that there is an apparent inconsistency in the fact that we found that a blond subject suffered only mild erythema after eighty minutes' exposure, while they found that at the intensity which *they assumed* that we used an intense erythema was produced on the inner aspect of the arm of a blond human subject with an exposure of fifteen minutes.

These criticisms were made on *their assumption* that we were using 56.43 ("33 clicks × 1.71 microwatts per sq. cm. per click at 1 meter") microwatts per square centimeter on the wound. As a matter of record, we have stated in two publications[11] that the intensity of radiation used by us has been 28 to 30 microwatts per square centimeter at the operative site. When this reported figure (approximately 50 per cent of their assumed but false figure) is taken into consideration, their work (so far as it goes, being entirely experimental, performed on bacteria and animals without clinical application) is a corroboration of the efficiency and safety of the intensity of radiation which we have used and advocated.

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11. Hart and others.[3] Hart and Sanger.[4]

12. Kraissl, C. J.; Cimiotti, J. G., and Meleney, F. L.: Considerations in the Use of Ultraviolet Radiation in Operating Rooms, Ann. Surg. **111**:161-185 (Feb.) 1940.

Our early work was done without the advantage of a meter for recording the intensity distribution of the radiation, so that exact measurements could not be given in our early publications. During the past three and one-half years, however, first with an assortment of equipment which was mounted on a supply truck and later with the compact meter which has since been developed by Westinghouse for simplification of the measurement of this radiation, the output of all radiation units, including the original experimental installation, has been checked regularly. The intensity distribution of each radiation unit as measured by a photoelectric cell sensitive to its predominant wavelength (over 88 per cent of the output at 2,537 angstrom units) and calibrated with a bismuth silver vacuum thermopile has been correlated with the distribution of bacteria as determined by the sedimentation method.

A number of different arrangements of ultraviolet radiation units have been tried, the results on four of which were demonstrated in a scientific exhibit at the meeting of the American Medical Association in Atlantic City, N. J., in June 1937 and have been on continuous exhibit in the Duke Hospital operating suite since that time. Only one of these gave more than 34 microwatts per square centimeter at the operative site,[13] and use of this was discontinued after a few trials because of the difficulty in protecting the personnel. There was, however, with this higher intensity no evident injury to any patient. The unit which we have used most during the past three years and which we are using exclusively, except for one of the new units developed by Westinghouse which we have recently installed, gives an intensity of 25 microwatts per square centimeter at the operative site, with a reduced intensity on the heads of the operating team and a higher intensity in all other parts of the room (floor, periphery and upper air) as compared with the other installations which we have tried. This unit, which delivers the least radiation on the wound, has been the most effective in reducing the number of viable sedimenting bacteria in every part of the operating room, including the operative site. These data, illustrating the desirability of effectively irradiating the entire room, were given to Westinghouse for the development of the unit which they have recently made available. Publication of the intensity distributions and bactericidal effect of these various installations has been withheld in order to include studies on this new unit. These data will be published at an early date.

13. All the intensities given are the actual measurements without any obstruction to the rays. During use in an operation it is estimated that from 15 to 25 per cent or more of the radiation is kept from the region of the wound by shading. Any tissue not on a flat exposed surface would receive less than half of the intensities given by measurements made without any obstruction.

SAFETY OF PERSONNEL

In regard to the danger to the operating room personnel, there are two risks to be considered, those due to acute exposures and those following often repeated slight or more prolonged exposures over a long period. Irritation of the skin from either type of exposure can be avoided easily by adequate covering or shading. The eyes can apparently be adequately protected by glasses and a close-fitting eye shade or hat, or, if one desires to be certain that no ray reaches the eyes, goggles can be worn. I have never seen a blister form on a patient or a member of the staff, and many of the nurses, anesthetists and orderlies do not cover their arms, necks or faces, wearing only glasses and a sun helmet in addition to the usual cap and mask. A few persons wearing no protection whatever have had conjunctivitis of sufficient severity to require local anesthesia, but this has always cleared within one or two days, without evident sequelae.

The possibility of chronic changes in the skin due to long-continued repeated exposures cannot be foretold. Experimental workers who have been exposed frequently for years report no ill effect. No harmful effect has been noticed on any of our staff. For the sake of safety, however, since the skin and eyes can be so easily shaded, every one using ultraviolet radiation should avoid unnecessary exposure until the risk of often repeated exposures over a long period is known. The rays have little power of penetration, closely woven starched cloth being sufficient to stop over 99 per cent of them, so that protection is relatively easy.

In order to simplify the protection of the personnel, certain of the radiation tubes in the units which we are now using have been placed at a higher level (10 feet 6 inches [above the floor]). Their output has been increased so as to give a slightly diminished intensity on the wound, a greatly diminished intensity on the heads of the personnel, a higher intensity at the floor and at the periphery of the room and a much higher intensity in the upper parts of the room, where the bacteria are carried by the convection currents. Not only does the additional height of these units as compared with the lower ones give a lower intensity on the heads of the personnel, but the ray which strikes them comes from a more nearly vertical direction, thus simplifying the problem of shading the eyes, the bridge of the nose and the adjacent skin.

SUMMARY

In approximately 2,000 clean incisions for operations of greater magnitude in the general, thoracic, urologic, orthopedic and neurologic surgical services performed in a field of bactericidal radiation, no patient has died as a result of an infection in the wound.

During the past year bactericidal radiation was used for 606 such clean primary incisions in a total of 6,535 operations of all types, with an infection rate of less than 1 per cent. Several of these infections probably were not received in the operating room, and not one was severe.

The few infections reported have been mild or questionable, and the total has been 1 per cent or less for all operating room infections in clean primary incisions. Exclusive of thoracoplasties, and if stitch abscesses and separations of the skin with a superficial granulating area are not considered as operating room infections, the infection rate for all operations reported by my associates and me [14] has been less than one third of 1 per cent (cases 3, 4 and 6 in this report).

The intensity of radiation (over 88 per cent output at 2,537 angstrom units) used is much less than 30 microwatts per square centimeter when shading is taken into consideration, and for most of the recent operations the intensity at the operative site has been only 25 microwatts per square centimeter, without allowance for shading.

In a recent article on ultraviolet radiation in the operating room [12] our work was criticized on the false assumption that we used a radiation intensity of 56.43 microwatts per square centimeter instead of approximately one-half that intensity, as we had previously stated.[11] With this false assumption corrected to our published figure the criticisms are not valid, and the work, so far as it goes, confirms the effectiveness as well as the safety of the intensities of radiation which we have used and advocated.

Animal experiments previously published [4] indicate that the intensities which we have used will not damage the tissues of the wound during the time they would be exposed during any operation if precautions are taken to prevent drying and unnecessary exposure of the tissues to the air.

No patient has ever made any complaint referable to, or received any evident injury from, the radiation.

The personnel can be adequately protected without loss of efficiency, and they should not take the risk of frequent or prolonged unnecessary exposures. Despite instructions otherwise, our personnel have taken many liberties with the skin, without evident damage other than an occasional mild and transient erythema. Many of the nurses and anesthetists do not cover the customarily exposed cutaneous surfaces except for the usual cap and mask supplemented by a hat and glasses.

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14. All operations performed with bactericidal radiation have been reported with the exception of a consecutive block from the fall of 1937 to Nov. 1, 1938. This group has not been reported on, and so the records have not been reread in a search for slight infections which may not have been entered on the diagnosis when the patient was discharged.

The eyes *must* be protected by glasses, and a closely fitting eyeshade or hat. In a few cases of conjunctivitis brought on by neglect of this precaution local anesthesia has been required, but this condition has cleared within one to two days, without evident sequelae.

ABSTRACT OF CASES

CASE 1.—Bilateral indirect inguinal hernias of two years' duration in B. W., a 47 year old white man, were repaired with the patient under cyclopropane anesthesia, a silk technic being used. The Wassermann reaction was 4 plus, and the Kahn reaction, 1 plus. The virtual absence of elevation of temperature after operation is shown in chart 1. During the remainder of his stay in the hospital, no temperature higher than 37.3 C. (99.1 F.) was recorded. On the sixth postoperative day, when the sutures were removed, there was reddening about some of them, with small stitch abscesses. Three days later all evidence of the infection had disappeared, and convalescence was entirely uneventful. This is a case of reaction of the tissues to a foreign body with growth of cutaneous organisms about the sutures and not one of "operating room infection."

CASE 2.—A cerebellar approach through the old scar was made for a recurrent astrocytoma in J. N., an 18 year old white boy. Leakage of spinal fluid occurred

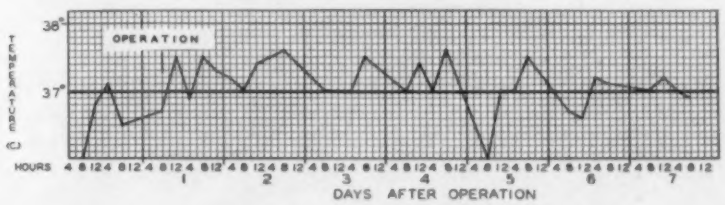

Chart 1.—Record of temperature in case 1.

on the fourth day following operation, and on the sixth day a stitch abscess was found at the right end of the incision. At this time leakage of spinal fluid had ceased spontaneously. On the eleventh postoperative day fluid aspirated from the wound contained 900 cells, and culture revealed Staphylococcus albus and a gram-negative bacillus. The patient was treated with sulfapyridine. On the seventeenth day following operation the wound again began to drain. The sinus tract was excised and closed, three galeal and three skin sutures of silk being used. The temperature curve for seven days after the major operation is shown in chart 2. During the subsequent course there were two short periods of elevation of temperature, one at the time of the wound aspiration and the other following rupture and secondary closure of the wound on the seventeenth postoperative day. Convalescence otherwise was uneventful, and the patient was discharged twenty-nine days after operation.

CASE 3.—A laminectomy was performed in J. M., a 25 year old Negro, ten hours after injury, through abraded skin, contused muscle and extravasated blood for a fracture dislocation of the first lumbar vertebra. The temperature curve for eight days after operation is shown in chart 3. The rise on the fifth and sixth days was caused by pneumonia, diagnosed by physical signs and confirmed by roentgen examination, and the organisms were identified by culture of the sputum as hemolytic yellow staphylococci. The patient was treated with sulfapyridine.

On the sixth day, without his having been catheterized, a few white blood cells were first noted in the urine. On the seventh the wound, which was not tender, was probed, but no pus was found. On the ninth, the hemolytic Staph. aureus was cultured in material from the wound.

On the eleventh day the urine was described as grossly infected, and the hemolytic Staph. aureus was grown on culture, and an indwelling catheter was inserted. On this day a blood culture showed 1 colony of the hemolytic Staph. aureus per cubic centimeter.

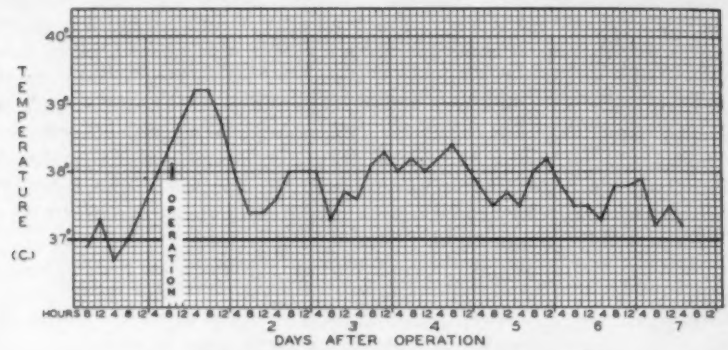

Chart 2.—Record of temperature in case 2.

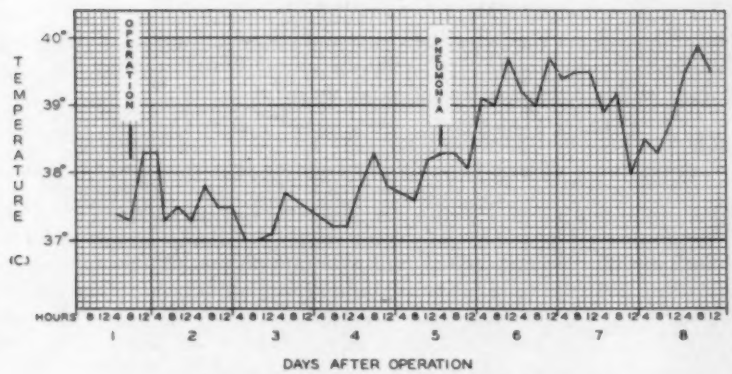

Chart 3.—Record of temperature in case 3.

The irregular temperature, reaching its peak on the eighth postoperative day, fell rapidly and from the twelfth to the thirty-eighth day was in general below 38 C., (100.4 F.) with irregular peaks somewhat above this. After the thirty-eighth day it remained below 38 C. The wound infection did not extend to the spinal canal, and the process in the chest cleared slowly, but the persistent moderate elevation of temperature was probably due to the infection of the urinary tract in a paralyzed patient.[15]

15. I consider that this wound infection was hematogenous and secondary to the pneumonia. During this twelve month period there were 2 other infections following operation (cesarean section and appendectomy) performed without

(Footnote continued on next page)

CASE 4.—W. L., a 27 year old white man with an ankylosis of the left hip, underwent an arthroplasty with insertion of a vitallium cup. A drain was inserted, and after operation there was a severe hemorrhage from the wound. The temperature curve for seven days after operation is given in chart 4. The drain was removed on the third postoperative day. On the ninth postoperative day the dressings were removed, and some superficial infection was present, cultures showing the hemolytic Staph. aureus. This is thought to have resulted from the hematoma in the wound with the persistent drainage tract. There was a rise of temperature to 39.5 C. (103.1 F.) on the ninth and tenth days, but the temperature dropped to normal by the twelfth day and remained below 37.5 C. (99.5 F.) for the next four and one-half weeks, or two weeks after motion and physical therapy were started. There was a slight rise in temperature then, but during the next twenty weeks there were only twelve recorded temperatures (temperature taken every four hours) above 37.5 C. and only one above 38 C. The cup was then removed. There was some granulation tissue about the cup but no destruction of bone. After this the patient's condition remained good, and nine weeks after removal of the cup he had 25 degrees of flexion, 15 degrees of extension, 15 degrees of adduction and 25 degrees of abduction.

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bactericidal radiation, and these infections were considered by me to have been hematogenous and secondary to pneumonia. A brief résumé of these cases follows:

An appendectomy for acute appendicitis (appendix unruptured) was performed on Sept. 4, 1939. On the second postoperative day there was bilateral bronchopneumonia. Sputum for culture could not be obtained. On the sixth day the incision was well healed, with no infection. On the seventh day there was pericarditis, with fluid in the right side of the chest. On the sixteenth day the incision was well healed. On the twenty-fourth day there was an abscess in the neck. On the twenty-fifth day an abscess developed at each venipuncture wound. There were abscesses also on the back, arms and neck. On the thirty-fifth day there was an abscess in the abdominal wall, involving the incision. On the forty-second day the temperature was normal and remained down for the remainder of the course in the hospital. On the sixty-seventh day the patient was discharged, recovered.

The patient was treated with sulfapyridine to the seventeenth postoperative day. The leukocyte count dropped to 1,950 per cubic millimeter by the twenty-third day. Staphylococcus antitoxin, 300,000 units, was given between the twenty-fifth and the twenty-eighth postoperative day. On the twenty-eighth day the leukocyte count was 12,850 per cubic millimeter, and by the thirty-second it was up to 20,800. All blood cultures were sterile. The urine did not become infected, and no sputum could be obtained for culture. All other cultures showed a pure growth of the hemolytic Staph. aureus. The temperature remained normal after the forty-second postoperative day.

A cesarean section was performed without bactericidal radiation on Nov. 1, 1938.

On the third day following operation the patient had pneumonia. The hemolytic Staph. aureus was grown on culture of the sputum.

On the tenth day the urine was infected with the Staph. aureus (hemolysis not noted).

The first evidence of wound infection was noted on the sixteenth day. Cultures showed the hemolytic Staph. aureus.

The patient recovered.

At the time of writing there is still a small sinus with a slight amount of discharge. The temperature was elevated for three days after the removal of the cup, and since that time has remained practically normal.

CASE 5.—Open reduction of a fracture dislocation of the ankle of three and one-half months' duration, with lengthening of the tendon of Achilles, was performed in L. E., a 43 year old Negro who had a psychosis during the postoperative course. Six days after operation he had conjunctivitis (hemolytic Staph. aureus). The cast was removed on the thirteenth postoperative day, and the skin, which had been closed with catgut, was found to be separated, with some superficial but no deep-seated infection. (Cultures were not made.) The temperature, which was as high as 37.7 C. (99.8 F.) before operation, is shown for seven days after operation in chart 5. During the next twenty days the temperature reached 38.1 C.

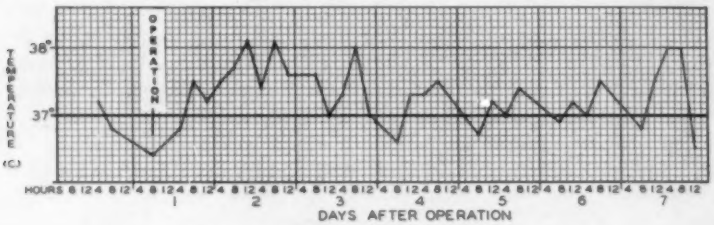

Chart 4.—Record of temperature in case 4.

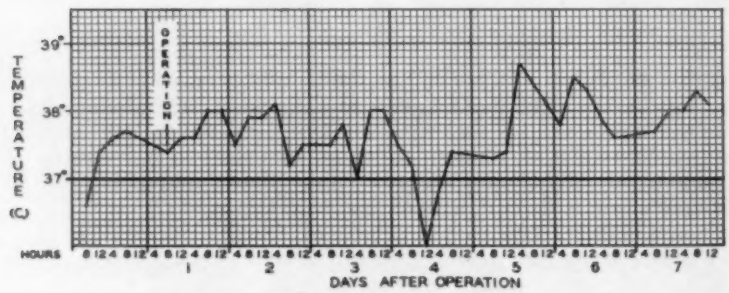

Chart 5.—Record of temperature in case 5.

(100.5 F) on three, 38.2 C. (100.7 F.) on three and 38.4 C. (101.1 F.) on two occasions; otherwise it remained at or below 38 C. Only the superficial part of the wound exposed by the separation of the skin was infected, and the patient was known to harbor the hemolytic Staph. aureus (conjunctivitis).

CASE 6.—A. A., a 26 year old Negress with tuberculosis of the right lung of fourteen months' duration underwent resection of the three upper ribs with apicolysis. During the freeing of the apex an enlarged lymph node was encountered and removed.

On the ninth postoperative day the wound was probed, and what was apparently a liquefied hematoma was evacuated. Cultures showed Staph. aureus and Staph. albus. In the next note (two days later) and in all subsequent notes the wound was described as clean and dry without drainage on the dressings. The temperature curve is shown for seven days in chart 6, first stage. There was a very gradual fall in temperature to the twenty-fifth postoperative day, after which the reading remained below 37.5 C. (99.5 F.).

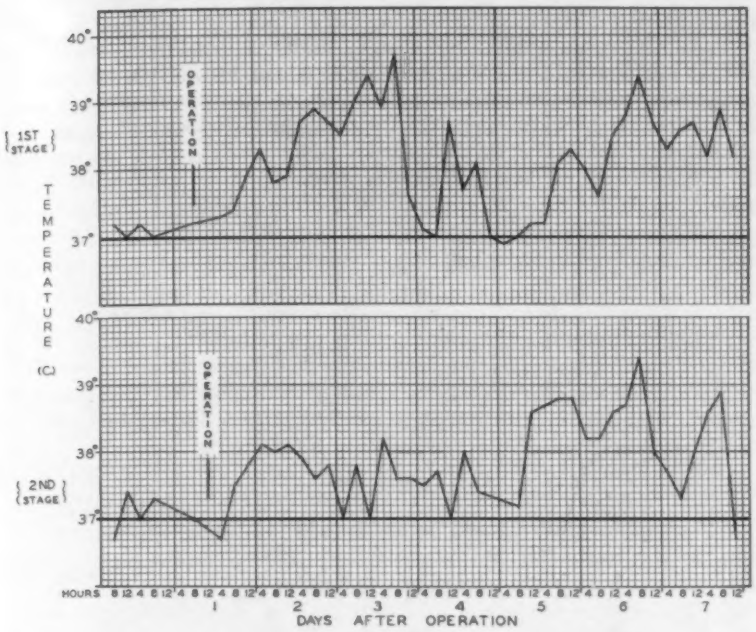

Chart 6.—Record of temperature in case 6.

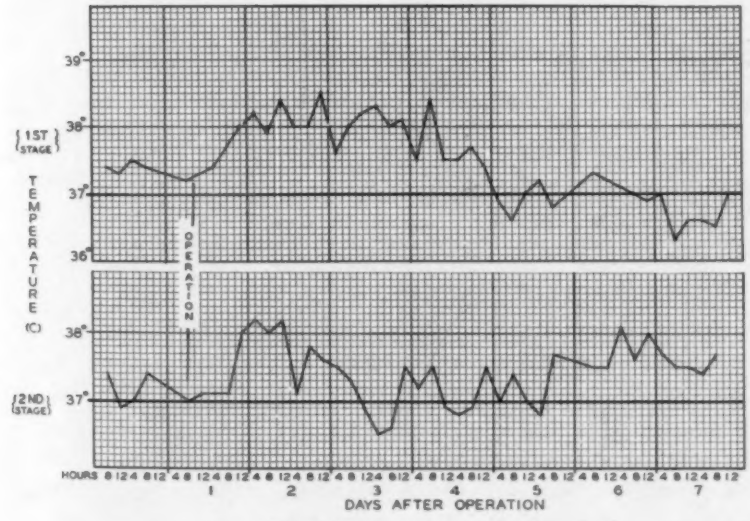

Chart 7.—Record of temperature in case 7.

The second operation, resection of parts of the fourth through the seventh ribs, was performed thirty-one days after the first stage. The operative note reports the excision of an ulcer in the old scar, although the preceding notes had reported that the wound was dry and that there was no drainage. There was no evidence of infection at the second operation, but cultures of material from the depths of the wound showed the hemolytic Staph. aureus. The temperature curve for the first seven days following operation is shown in chart 6 (second stage). The temperature remained below 38 C. after the eighth day. On the seventh postoperative day, 100 cc. of bloody fluid was evacuated from a hematoma in the incision, and on the ninth day cultures showed the hemolytic Staph. aureus. Bloody drainage continued to the twentieth day, and on the twenty-sixth day all drainage had stopped. On the thirtieth day after operation there was only a superficial unhealed area 3 mm. long.

In the first stage the wound was not considered by the operator to be infected, the elevation of temperature being explained as due to pulmonary spread, but the subsequent culture reports make the diagnosis of infection conclusive even though it may not have been responsible for the elevation of temperature. The reason for performing the second operation when an ulcerated area had to be excised in making the cutaneous incision for the second stage was not given. The second stage operation should have been postponed. The field was evidently infected by viable organisms persisting in the wound from the infection in the first stage.

Case 7.—C. B., a 42 year old white woman with tuberculosis of the right lung of four years' duration, underwent resection of the upper three ribs with apicolysis. The postoperative course was uneventful, the wound healing without evidence of infection. The temperature curve for seven days after operation is shown in chart 7 (first stage), and from this time until the next operation the temperature remained below 37.5 C.

The second stage, with resection of parts of the fourth through the sixth ribs, was performed fourteen days after the first stage. There was a large pocket of fluid in the defect left by the apicolysis. On gross inspection this was apparently uninfected, but cultures revealed the hemolytic Staph. aureus. When the sutures for the second stage were removed on the seventh day there was an escape of "20-30 cc. of dark blood and fat droplets." Cultures showed the hemolytic Staph. aureus. Drainage of chocolate-colored material continued to the thirteenth day, and on the twenty-sixth day all drainage had ceased. The temperature curve for the first seven days after operation is shown in chart 7 (second stage). During the subsequent course in the hospital (thirty-seven days after operation) the temperature did not go above 37.6 C. (99.6 F.).

CONTRIBUTION OF THREE EARLY BRITISH SURGEONS TO KNOWLEDGE OF HEART DISEASE

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The primary motive that has induced me, an internist, to accept the kind invitation to have a share in this special number of the ARCHIVES OF SURGERY is that by so doing I may show my appreciation of, and affection for, Dean Lewis. To have known him as a student, intern, faculty and hospital colleague and congenial companion is to have an abiding sense of his superior ability as a surgeon, teacher and medical leader, and of his genius for making and holding friends.

I trust it may not seem inappropriate to reiterate in this paper the truth that medicine and surgery are, and should be, closely related and mutually helpful, and, as a concrete illustration of the debt owed by medicine to surgery, to call attention to the worth while contributions made to the knowledge of heart disease, a little more than a century ago, by three British surgeons.

At that time, in the early eighteen hundreds, when nothing was known of bacteriology, anesthesia or x-rays; when at the bedside practically no use was made of the microscope or of chemistry; when there was no auscultation or application of electricity in diagnosis or treatment, the well educated medical man possessed and utilized a much larger proportion of the existing medical knowledge than is possible today. Dividing lines between different types of practitioners were not so sharply drawn as they are at present. There were really but two outstanding specialists: the physician—the internist—and the surgeon, though many were known as obstetricians and the ophthalmologist and the dermatologist were bidding for recognition. As a matter of fact, the surgeon was but the physician who was distinguished by his more accurate knowledge of anatomy and his dexterity as an operator. At the bedside and at the necropsy table, as well as at operations, the surgeon made observations that had a bearing that was general and not limited to his own specialty. As an example may be named John Hunter. That the process was a reciprocal one is shown by the work of such an internist as Edward Jenner. Happily, this mutual interchange of knowledge is still going on between medical specialists of every type and between medicine and cognate sciences, like chemistry, physics and

biology. It is one of the chief agencies that are tending to make medicine more nearly an exact science.

The three British surgeons were Joseph Hodgson of England, Allan Burns of Scotland and Robert Adams of Ireland.[1] While their contributions are of minor grade, they are yet of value. It is remarkable that the authors were relatively young at the time they wrote: Hodgson in 1815 was 27; Burns in 1809 was 28; Adams, writing in 1827, was older, though only 35.

Allan Burns, son of the Rev. John Burns, was born in Glasgow, Scotland, on Sept. 18, 1781. He was precocious. At 14 he began to study medicine. At "sixteen he took upon himself the sole direction of the dissecting rooms of his elder brother, John Burns, who at that time was an extramural lecturer on Anatomy and Surgery at Glasgow" and who was later the author of a popular work on obstetrics. Allan "soon made for himself a reputation as a practical anatomist." Unlike his brother John, he did not excel as a lecturer, but as a demonstrator and dissector he was *facile princeps,* with an enthusiastic following of students. He studied disease also, both in the wards of the infirmary and in the morgue. Not having a university degree, he had to obtain his experience as physician and surgeon chiefly by attending and studying the patients of his brother and of his friends. He had no practice of his own. In his case books he made notes and drawings that stood him in good stead when later he wrote on the diseases of the heart, on the blood vessels, on surgical anatomy and on hernia. After an illness that one recognizes today as a recurring appendicitis, he died on June 22, 1813, when he was 31 years and 9 months old. His death, terminating a brief but brilliant career, was, in the words of Duncan, "a severe blow to the Glasgow Medical School on which he had already shed lustre."

The first of the major works of Allan Burns was his "Observations on Some of the Most Frequent and Important Diseases of the Heart; on Aneurism of the Thoracic Aorta; on Preternatural Pulsation in the Epigastric Region; and on the Unusual Origin and Distribution of Some of the Large Arteries of the Human Body. Illustrated by Cases." This was published in Edinburgh in 1809. In 1811 appeared his "Observations on the Surgical Anatomy of the Head and Neck. Illustrated by Cases and Engravings." In addition to these books he contributed to medical journals several articles, chiefly surgical, that need not be mentioned here.

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1. In writing this paper I quote freely from articles on Allan Burns (Herrick, J. B.: Allan Burns: 1781-1813, Anatomist, Surgeon and Cardiologist, Bull. Soc. M. Hist. Chicago **4**:457-483 [Jan.] 1935; Robert Adams, Surgeon, and His Contributions to Cardiology, Ann. M. Hist. **1**:45-49 [Jan.] 1939) that are already in print.

A few of the more outstanding features of Burns's book on heart disease will be noted. He gave accurate anatomic descriptions of congenital anomalies and showed an intelligent understanding of the resulting disturbances. He discussed pericarditis in a fairly satisfactory manner. His anatomic diagnosis was clearcut. He described what is today called pericarditic mediastinitis when he referred to complete "matting" of the pericardium with the neighboring parts. He explained some of the signs, such as a "diffused undulation" rather than a decided pulsation, on the basis of adhesions to the diaphragm and other structures. He was explicit in emphasizing the reference of pain to parts other than the pericardium, such as the epigastrium or the shoulder. Again: "Where also no change takes place in the spot where the pulsation is felt in the chest, when the patient turns from side to side we are assisted in our diagnosis" of adhesive pericarditis. Had Burns known of auscultation, percussion, bacteria; of albuminuria as evidence of renal disease, and of the importance of clinical thermometry, his description of pericarditis would have been equal to any written today.

In reading Burns, one is impressed by the broadness of his views, such as his conception of the unity of the heart and blood vessels, the modern notion of the cardiovascular system. He was anatomist, physiologist and pathologist as well as internist and surgeon. "Until," he said, "we possess clear notions respecting the natural functions of a part, our ideas concerning its morbid actions, can never be otherwise than vague and unsatisfactory. But often our opinions regarding healthy function are corrected by observing what takes place in disease."

Chapter 7, on disease of the coronary arteries and on syncope anginosa, is of special interest to cardiologists, for it contains Burns's statement concerning the myocardial ischemic theory of angina pectoris. With characteristic frankness Burns acknowledged his indebtedness to others and his unqualified adherence to the coronary artery theory of angina pectoris. "To Drs. Hebberden, Jenner and Parry, we owe most of our information respecting this most fatal complaint," a condition which Parry "has incontrovertibly proved to originate from some organic laesion of the nutrient vessels of the heart."

He compared the heart with obstructed coronary vessels to a limb with a ligature. The limb can continue in vigorous action for only a short time; then weakness enforces rest. The heart "is principally composed of muscle and we have therefore reason to believe that it is regulated by the same laws which govern other muscles" (p. 143). The heart, like every other part of the body

> . . . has peculiar vessels set apart for its nourishment. In health, when we excite the muscular system to more energetic action than usual, we increase the circulation in every part, so that to support this increased action, the heart

and every other part has its power augmented. If, however, we call into vigorous action, a limb, round which, we have with a moderate degree of tightness, applied a ligature, we find that then the member can only support its action for a very short time; for now its supply of energy and its expenditure, do not balance each other; consequently, it soon, from a deficiency of nervous influence and arterial blood, fails and sinks into a state of quiescence. A heart, the coronary vessels of which are cartilaginous or ossified, is in nearly a similar condition; it can, like the limb be girt with a moderately tight ligature, discharge its functions so long as its action is moderate and equal. Increase however the action of the whole body, and along with the rest, that of the heart, and you will soon see exemplified, the truth of what has been said; with this difference, that as there is no interruption to the action of the cardiac nerves, the heart will be able to hold out a little longer than the limb. (P. 138.)

If a person walks fast, ascends a steep, or mounts a pair of stairs, the circulation in a state of health is hurried, and the heart is felt beating more frequently against the ribs than usual. If, however, a person with the nutrient arteries of the heart diseased in such a way as to impede the progress of the blood along them, attempt to do the same, he finds, that the heart is sooner fatigued than the other parts are, which remain healthy. When, therefore, the coronary arteries are ossified, every agent capable of increasing the action of the heart, such as exercise, passion and ardent spirits, must be a source of danger. (P. 139.)

Burns deserves credit as an early advocate of Parry's [2] theory of a lesion of the coronary artery and relative myocardial ischemia in angina pectoris and for having made a crude experiment to substantiate his theory.

For a discussion and explanation of the fact that Burns in his description of his experiment and in his application of the results of this test to conditions in the human heart stressed weakness and syncope rather than pain as the major cause compelling cessation of muscular action in the limb or heart, as well as for the comments of MacMillan and Webster (1923) and Sir Thomas Lewis (1932) on this feature of Burns's experiment, I refer the reader to pages 14 and 16 of my article on Allan Burns.[1]

In reading chapter 8, called "Observations on the Effects Resulting from Change of Structure of the Valves of the Heart and Large Arteries," one is impressed by the modernness of Burns's views. One sees also that he was more than a mere morphologic anatomist; that he was a pathologist who aimed to correlate judicially the clinical and the pathologic findings. "We are not," he said, "in every case, where after death we find these appendages—the valves—opaque, to conclude that this change from the healthy transparent state, shall have been accompanied with a correspondent alteration in the function" (p. 163).

He described a case of what today would be recognized as mitral stenosis with auricular fibrillation and congestive heart failure. The

2. Parry, C. H.: An Inquiry into the Symptoms and Causes of the Syncope Anginosa, Commonly Called the Angina Pectoris, London, Cadell & Davis, 1799.

presystolic thrill, the sharp systolic impulse, the pulse deficit are all there as evidence of his accurate clinical observation. What is lacking is auscultation. The autopsy revealed the constricted indurated valve.

One of the best chapters is the ninth, on the formation of polypi in the heart. He made a clear distinction between antemortem and postmortem clots, calling attention to differences in consistency, color, attachment to the wall of the heart and the like.

Burns discussed in a scholarly and scientific manner aneurysm of the thoracic aorta. This chapter reveals an extensive search of the literature, a careful survey of his own cases and a clarity, directness and conciseness in style that show more revision than is apparent in some of his other chapters. He considered pathogenesis, in general agreeing with Scarpa. He had experimented with rupture by injecting wax into the artery. The symptoms, which were fully discussed, were always interpreted in terms of anatomy. Unequal pulses, dysphagia and swelling of veins were considered not merely curious or mysterious phenomena, for "there must be some physical reason for this diversity of effect" (p. 243).

The substance of the chapter on the causes of preternatural pulsation in the epigastrium may be learned from the summary at the end of the chapter: "Pulsation *in epigastrio* may be produced by adhesions of the heart to the pericardium; by enlargement of the heart itself, chiefly of the right side; by tumours attached to the diaphragm; by enlargement of the vena cava inferior; by preternatural solidity of the lungs; by any solid increase of substance about the aorta; or roots of the large abdominal arteries; and lastly by a peculiar affection of the vascular system itself" (p. 276). In the latter condition, to judge from the histories presented, may have been included cases of exophthalmic goiter, severe anemia and, possibly, neurasthenia. There was a recognition of the so-called positive hepatic pulse.

His concluding chapter, of forty pages, was headed "Remarks on the Unusual Origin and Course of Some of the Large and Important Arteries of the Human Body" and was based on the observations and records made by Burns during his many dissections of the preceding several years. "All the descriptions, with the exception of a single one on the authority of my friend, Dr. Barclay, are taken from dissections made by myself or from preparations in my possession" (p. 322). Perhaps Granville Pattison did not exaggerate when he said that Burns's collection of vascular preparations was, at one time, superior to any other in the world.

In 1811, when he was 30 years old, Burns published his observations on the "Surgical Anatomy of the Head and Neck, Illustrated by Cases and Engravings." Its style was less discursive than that of the volume on the heart. The volume is packed with suggestions on practical sur-

gery; it might be spoken of as a work on anatomic surgery rather than surgical anatomy. A great variety of topics with illustrative cases was taken up: esophagotomy, resection of the trigeminal nerve for tic douleureux, ligation of thyroid arteries for bronchocele, melanotic tumor of the eye with metastasis to the liver, etc. The work was highly regarded by Burns's surgical contemporaries and his immediate successors. Valentine Mott referred to the author as "this celebrated anatomist." Complimentary references were made by Abernethy and Sir Astley Cooper. Meckel, in a foreword to the Halle translation of 1821, spoke of it as not merely a compilation of known facts but a work that enriched the science and art of medicine through original observations and investigations. Duncan, in 1896, said: "His work on the *Anatomy of the Head and Neck* is one of the most noteworthy contributions to anatomy which the Glasgow School has yet made." A second edition was published in Glasgow in 1824 and in Edinburgh in 1833. An American edition appeared in 1823.

The work of Burns cannot be regarded as epoch making, as was that of Laennec, for example, or that of Jenner. Yet his writings contain many evidences of such keen insight into facts and causes that one is tempted to speak of them as prophetic. Some were genuine contributions to knowledge, not always entirely new, but presented from a new point of view or with some illuminating addition. The coronary artery theory of angina pectoris and his experiment with the ligature, his clear statement of the back pressure theory of dilatation and hypertrophy whether from valvular obstruction or leakage and his discussion of antemortem thrombi and aortic aneurysm were notable contributions. He had the spirit of investigation—witness his careful records and specimens of arterial anomalies, his work on epigastric pulsation, his injection of arteries to show collateral circulation, his thorough postmortem examinations and his correlation of clinical and pathologic observations.

His treatise on heart disease, with all its faults, was pioneer. His book on surgery of the neck was an advance over anything previously published. He was progressive and capable of growth. Had he lived to know of Laennec and Louis, of Skoda and Rokitansky, he would, whether practicing and studying as a surgeon or as an internist, have been one of the leaders among the choice group of British clinicians whose names add brilliancy to the first half of the nineteenth century, a group containing, among others, such men as Stokes, Bright, Addison, Graves, Astley Cooper and Paget.

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In 1811 Joseph Hodgson (1788-1869), then a young man of 23, was awarded the Jacksonian prize of the College of Surgeons of London for his essay on "Wounds and Diseases of the Arteries and Veins." A

supplementary paper with illustrative cases was presented in the same year. These two contributions, so he said, were the basis of his work published in 1815, "A Treatise on the Diseases of Arteries and Veins, Containing the Pathology and Treatment of Aneurisms and Wounded Arteries." [3]

Hodgson, a surgeon, naturally considered aneurysm, varicose veins and wounds of blood vessels chiefly from the surgical point of view. The symptoms, signs and diagnosis, together with the dangers and natural history of untreated conditions and the various plans of treatment, were minutely described. He gave details as to ligation of various arteries. He cited his own experience and that of others made familiar to him by a thorough search of the literature. Yet one errs if one thinks Hodgson's interests were purely surgical. One of the striking features of the book is that his views were comprehensive. He discussed in a thorough and scientific manner the gross and microscopic pathologic processes in the arterial wall that lead to or accompany aneurysm. He recognized the close relation between lesions seen in the diseased aorta and the coincidental changes in the neighboring valves and coronary arteries of the heart. He submitted some of his experimental work. As an important manifestation of disease of the aortic wall he described cylindric dilatation of the arch without saccular aneurysmal bulging. He referred to the fact that this condition is often seen in those who have had syphilis and raised the old question whether syphilis or the mercury used in its treatment is responsible for the trouble. Today, when the relation of syphilis to a diseased and dilated aorta, often with accompanying aortic valvular incompetency, is better understood, the French frequently refer to the condition as *maladie d'Hodgson,* thus acknowledging the pioneer character of this important work.

One marvels at the scholarly manner in which this book was written, the unusual ability of the young writer of 27 in exposition and argument; the clarity, the purity of his English, the orderly presentation. The frequent summaries are as clearcut, as concise and as logical as a good lawyer's brief. His accurate bibliographic references show that he had made an exhaustive search of the literature of the time.

A separate quarto volume contains the eight plates after drawings by Hodgson. Six were engraved by J. Stewart; two, by J. Shury. These plates were made up of twenty-four figures. The drawings and the engraving, as well as the printed pages of legends, are beautiful examples of the best book making and illustrating of those days.

That Hodgson's interest was not restricted to aneurysm may be seen when one notes a few other topics that he touched on, some very briefly,

3. London, T. Underwood, 1815.

others more fully. He described valvulitis (p. 7), postmortem staining (p. 8) and aortic regurgitation (p. 15). One recognizes in his case III, with its plate and accurate description (p. 18), a typical instance of what is today called bacterial endocarditis. He had a clear conception of the interference with function caused by atheroma in the aged (p. 24). He depicted the calcareously obstructed aortic valve and contrasted this with mitral stenosis. In the latter condition he recognized a bruit, also a heart pulse that in 1 instance was double that which he felt at the wrist (pp. 28-33).

He was familiar with the views of Jenner and Parry as to the relation of angina pectoris to disease of the coronary artery, though his conception of the peculiar substernal distress to which the term angina was applied was not as clearcut as that of Parry, Jenner or Heberden. He recognized the fact that altered coronary arteries may be a cause of heart disease, citing 3 cases in which these vessels were found to be sclerotic and markedly obstructed. Thin-walled ventricles, and in one case rupture, had resulted from this condition (pp. 37-40). He described a case of aneurysm of the heart with an intraventricular thrombus, probably from an old infarct (p. 84). He recognized what is now spoken of as relative aortic regurgitation (p. 50). He offered proof of the rapid compensatory dilatation of minute and previously invisible anastomotic branches in cases of aneurysmal or ligational obstruction (pp. 237-238), which recalls the later work of Krogh. He referred to cases reported by others that sound like coarctation of the aorta (pp. 250-251). He described phlebitis with the thrombi and drew a striking picture of cases in which septic phlebitis had followed infection at the time of a venesection or in connection with parturition (pp. 513-517).

These features of his monograph, especially his description of what is now usually spoken of as syphilitic aortitis (Hodgson's disease), were distinct contributions to the pathogenesis and clinical features of cardiology. They had, and still have, an interest for the nonoperating physician, i.e. the internist.

It is worthy of note that Hodgson made his reputation not in the metropolis, but in provincial Birmingham, the city of his birth. He was known as "Hodgson of Birmingham." Here, for thirty years, he was engaged in an enormous and lucrative general and consultation practice. In 1824 he founded the Birmingham Eye Infirmary. He was regarded as a skilled operator on the eye. He had an enviable reputation as a genitourinary surgeon. He had cut for stone in the bladder 86 times, losing only 4 patients. He was an early advocate of lithotrity. In 1849, with ample means, he withdrew to London. He had no desire to engage further in practice, though he was occasionally consulted by his old

patients. He became active in various medical organizations. In 1864 he was president of the College of Surgeons. He died in 1869 at the age of 81, highly regarded by patients and colleagues as a man, a physician and a surgeon.

Some frank comments on his character and ability were made later by Sir William MacCormac in his address of welcome as president of the Royal College of Surgeons at its centenary celebration in 1900.[4] He referred to Hodgson as an able surgeon of the old school. "His diagnosis was accurate but cautious." He was not a brilliant operator. He was averse to innovations, medical or political. In his early life he was constantly involved in many quarrels. In later years he was remarkable for his "suavity and kindness of manner." He was referred to by another, Dr. Madden Stone, as "that mild gentle creature." One may infer that Hodgson was a forceful man, an all-around surgeon of the older, preaseptic school, of an investigative yet skeptical turn of mind, honest and careful and obdurate in defense of his own views. He evidently mellowed as he grew older. One may wonder whether his retirement to London and a quieter life was due entirely to the fact that he had grown tired of the strenuous practice and had accumulated all the wealth he cared for, or whether some sign of ill health warned him to slow up. The obituary notice in the *Lancet* (1869) said he was believed to have had for years a pulse rate of only 40.

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Much has been written of the remarkable group of men who in the first half of the nineteenth century made the Dublin school of medicine take rank close to the schools of Paris and Edinburgh. The internists included Stokes, Graves, Corrigan and Cheyne. They might not be so well known today were it not that their names are attached to certain clinical conditions that were given early and prominent notice by them—Graves's disease, Cheyne-Stokes respirations, Corrigan's pulse, Colles' fracture, Colles' law of syphilis, Stokes-Adams syndrome. Their fame, however, rests on a surer foundation than the fortuitous and fortunate circumstance of having the name attached to a disease or a symptom. These men deserve high rank for their real accomplishments.

Robert Adams (1791-1875), perhaps the least known of the group, was yet held in high esteem by his colleagues, as is shown by the fact that he held various hospital and college positions and was three times president of the Royal College of Surgeons of Ireland. He made many contributions to surgery, especially to the surgical knowledge of disease of the joints. In 1873, when he was 81 years old, he brought out "A Treatise on Rheumatoid Gout or Chronic Rheumatic Arthritis." With

4. MacCormac, W.: Address of Welcome, in Centenary of Royal College of Surgeons of England, London, 1900, pp. 134-135; Brit. M. J. **2**:209-212, 1900.

this there was a fine atlas of plates. The writer of an obituary in the *Medical Times and Gazette* referred to him as one highly regarded as a man, "a judicious surgeon," "to be considered as distinguished a physician as he was a surgeon."

The claim to distinction as a physician is based largely on an article of one hundred pages which Adams published in the Dublin Hospital Reports.[5] The title of his paper is "Cases of Diseases of the Heart Accompanied with Pathological Observations."

The first description of what is today called the Stokes-Adams syndrome is found in this article. This description has been quoted so often that it need not be repeated here. It clearly warrants one in crediting Adams with having first noted what was later called the Adams-Stokes syndrome. The name of Stokes is properly coupled with that of Adams because Stokes[6] in 1846 in an article in the *Dublin Quarterly Journal* wrote in a comprehensive manner of this type of permanently slow pulse in connection with heart disease. Stokes discussed the relation of all the phenomena to the condition of the heart and spoke of the symptom group as a "combination of a singularly slow pulse, tendency to syncope, and disease of the aortic valve." He concluded by saying that he published these observations made on 7 cases "with the view of drawing the attention of the profession to a combination of cerebral and cardiac phenomena, of which our knowledge is still imperfect."

Robert Adams, however, did much more than describe for the first time and in a somewhat casual manner the peculiar pulse and seizures now called Adams-Stokes syndrome. His article reveals him as possessed of a more than ordinary grasp of the clinical features of heart disease and the associated organic lesions together with the physiologic disturbances accompanying such disease. It is surprising to think that this expertness as a cardiologist was in a sense avocational, for Adams was primarily a surgeon. He represented the type of operator who was first a good all-around physician. Here are some of the features of this article that substantiate the statement.

Several cases of pericarditis were reported. Adams, who was fully aware of the fact that obstruction to the blood current, as from a narrowed valve, leads to increase in the musculature of the heart, said that in an analogous manner obstruction to the free working of the heart because of pericardial adhesions may lead to hypertrophy. But he had a new view as to the cause of such muscular increase:

> Although we not unusually find the heart enlarged where the pericardium is adherent to it this has never been, as far as I know, referred to as a cause of

5. Adams, R.: Dublin Hosp. Rep. **4**:353-453, 1827.

6. Stokes, W.: Observations on Some Cases of Permanently Slow Pulse, Dublin Quart. J. M. Sc. **2**:73-85, 1846.

its inordinate growth; yet when we reflect that in the natural state the heart has no vascular connexion with the surrounding organs, and is only supplied with two small arteries, we can readily conceive what a new impulse its nutrition must derive from the immense number of vessels which from the adherent pericardium will pass directly into the muscular substance of the heart. Under such circumstances we may fairly attribute enlargement of the heart to the pericardium, as the unlimited growth of a tumour to the organised cyst which contains it.

This, it will be noted, is the basic conception that underlies certain operative procedures of today for improving the circulation in a damaged myocardium by artificially inducing adherent pericardium.

His description of the phenomena of mitral stenosis is such as only a careful and well informed clinician could write. The thrill, the arrhythmia and the pulse deficit are there; the phenomena in the jugular and other veins are described. The essence of King's safety-valve effect in the giving way of the right side of the heart was clearly appreciated. His explanation of the phenomena of the jugular pulse was based on accurate studies of the veins and heart both before and after death. Stokes in his generous way gave Adams credit for having made the first and the most important contribution to the subject of contraction of the mitral valves since the time of Laennec.

Adams came close to, but really missed, recognition of acute coronary obstruction as a cause of myocardial softening. He discussed rupture of the heart muscle, citing a case reported by Dr. Cheyne, the symptoms of which would today be recognized as those of coronary thrombosis. The autopsy showed the muscular fiber of the left ventricle "remarkably soft in its structure so as to admit of being broken down between the finger and thumb." Death had been due to hemopericardium caused by a rupture of the wall of the left ventricle through this softened area. Adams cited a second instance of rupture of the ventricle reported by his surgical colleague, the celebrated Abraham Colles.

But Adams came closer than this to discovering coronary thrombosis as the following epitome of his words will show. He presented a masterly discussion of ossification of the aortic valves and contraction of the aortic opening. The thrill and murmur were noted, as were the effects of this lesion on the pulse. He clearly recognized a difference in etiology between aortic obstruction in the young and the old—a juvenile or inflammatory versus a senescent degenerative type. In this connection he reported a case unique in his experience. A fleshy man of 68 had been seized with a severe pain in the chest that ran down the right arm, numbness, dizziness and dyspnea. There was no pulse in the right wrist and a weak pulse in the left. The next day and for seven weeks, or until death, no pulse could be felt in any artery; "an obscure undulating motion could alone be heard when the ear was for some moments attentively applied to the side of the thorax." A diagnosis of heart disease was made, the exact nature unknown.

At the examination made the day after death "the heart was large, flabby and of a yellow color from fatty deposition." The semilunar valves of the aorta were "completely ossified. But this bony or earthy deposition was not confined to the aorta; it extended to the coronary arteries so completely converted into bone as to be quite solid, having no perceptible cavity except at the distance of an inch from their origin; beyond this the vessels were at intervals completely interrupted by small bony specks."

Those present at the dissection were puzzled to understand the symptoms, especially the absence of the pulse, most feeling that the condition of the aortic valves explained all, i.e., that only an insufficient blood supply could get through the narrow orifice. But Adams said that he had seen several other cases of aortic stenosis in which, while the pulse had been small, it was always to be felt. He concluded that some other cause contributed to this effect and believed it was found in the obstructed coronary arteries. He argued that in other muscular organs, if the natural blood supply is cut off, paralysis, partial or complete, follows.

> When we reflect that the heart can derive no supply from any other source than its coronary vessels, it will not appear then so extraordinary that partial paralysis should be the immediate consequence of the complete obstruction of these channels upon which the heart is evidently so dependent. The paralysis, if we dare so denominate it, was not in this instance, and indeed seldom is in any case, so complete as to deprive the muscular organ of all power of motion. The heart was still just capable of contracting, and thus passing onwards the blood it received, but so feeble was its impulse that the slightest motion was not perceptible in any branch of the arterial system.
>
> It is evident that there must have been something mechanical in the cause which thus impeded the action of the heart.

A few sentences later he said: "The suddenness of the cessation of the pulse precludes the possibility of our accounting for it on mechanical principles." Apparently he meant that there was no permanent mechanical obstruction of the radial or other peripheral arteries. Adams regarded the case as an irregular form of angina pectoris. He concluded: "Thus, although we can have but little doubt that in the case we have just been considering the organic seat of the gentleman's complaint was to be found in an ossified condition of the coronary arteries of the heart and aortic valves, we are not by such a consideration furnished with any certain means of knowing why the pulse suddenly ceased in every artery in the body at a time when the general health seemed unimpaired."

One cannot help thinking that had the myocardium been examined more carefully evidence of recent damage might have been discovered; more thorough search in the coronary vessels would have revealed the

offending thrombus. As it was, by exceptionally clear, logical reasoning Adams came close to discovering the true nature of cases that today are not so mystifying as they were a hundred years ago.[7]

Adams was far from being a lesser light in the Dublin galaxy. He was of greater brilliancy than has been generally recognized. He had in him the elements of the true clinical investigator and deserves most honorable mention in any history of cardiology.

122 South Michigan Avenue.

7. Some may question the fact that a patient with acute coronary occlusion can live for days with no perceptible peripheral pulse. I am sure, however, that this is possible. I observed 1 case in which no radial pulse could be felt for six or eight hours before death, the patient being quite conscious during this time. In another patient who lived for five weeks after the coronary accident there was never felt during this period more than a rapid, extremely small thready radial pulse. For hours at a time neither the nurse nor the physician could feel it at all.

INCIDENCE OF SUBSTERNAL AND INTRATHORACIC GOITERS

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Substernal and intrathoracic goiters differ only in degree. In the present series, when the major portion of a goiter occurred above the sternum, with only prolongations extending below it, the growth was classified as substernal, and when an entire adenoma was below the level of the sternal notch it was classified as intrathoracic. In the past ten years 173 substernal and intrathoracic goiters have been encountered, and during that same period, 1,334 operations on the thyroid were performed, giving an incidence of 12.9 per cent of abnormally situated goiters. Nine of the 173 patients, or 5.2 per cent, had had one or more previous operations on the thyroid gland, varying from eight months to twenty-one years. The recurrence of eight months was undoubtedly present at the time of the first operation, but the recurrence occurring twenty-one years after the first operation may or may not have been present at the time of the first operation. One patient had had three operations within three years for the same symptom—pressure—before being relieved. The first and second operations had removed practically all of the normally situated thyroid without the intrathoracic tumor even being suspected.

REPORT OF CASES

CASE 1.—E. K., a single woman aged 60, was seen in March 1931. She had undergone the menopause at the age of 42.

Thyroidectomies had been performed in June 1927 and June 1929.

The patient had for years been subject to "strangling spells" and headaches, especially if she changed her position quickly. She did not become cyanotic but had difficulty in getting her breath. She complained of tenseness and spasm of the chest with these spells. She complained also of a spastic, irritable bowel. She had been under treatment for this complaint for over a year. The blood and the urine were within normal limits; the Wassermann reaction was negative. The blood pressure was 128 systolic and 76 diastolic. The pulse rate was 80. No thyroid tissue was palpable. There were no rales. There was dulness in the upper part of the left side of the chest. The breath sounds were clear. The abdomen was full and tender.

Roentgen Examination.—The superior mediastinum showed a large tumor mass, with displacement of the trachea and the esophagus to the right. The mass had the appearance of a substernal thyroid.

Diagnosis.—The diagnosis was intrathoracic goiter and spastic colon.

Course.—The patient was operated on in March 1931. Procaine hydrochloride and ethylene were used. The tumor was attached to the lower pole of the remaining left lobe. In removing the tumor the pleura was opened with a small amount of hemorrhage. One large pack was left in the neck for four days and, removed gradually. There was no bleeding.

A roentgenogram taken on May 1 (fig. 1*B*) showed the lung fields to be clear. There was no substernal shadow. This case illustrates the absolute necessity of roentgen examination in diagnosis. Figure 1 illustrates the condition before and after operation.

The manner of production of substernal and intrathoracic goiters has been a subject of discussion, but with an adenoma from the lower portions of either lobe and considerable pressure above of muscles or a low-lying thyroid gland, it is easy to see this gland develop in the line

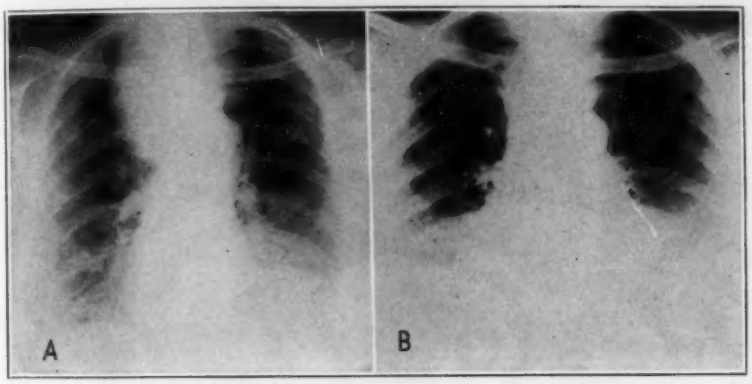

Fig. 1.—Condition (*A*) before and (*B*) after treatment.

of least resistance, and after being "hooked" below the sternum it can develop only downward. Also, the influence of swallowing tends to direct the growth downward.

The enlargements were evenly divided as to location; 61 occurred on the right and 60 on the left, with 7 on both sides and no mention made of the situation of the remainder. There was no case, however, in which the intrathoracic extension was completely separated from the lobes above, as with an aberrant thyroid.

SYMPTOMS

The predominating symptoms were cardiac disturbances and pressure with dyspnea, husky voice, tumor and enlarged veins (case 2 [not described], fig. 2) over the neck and upper part of the chest, in the order named (cardiac disturbances to include the cardiac signs incident to the toxic nodular type of goiter). Again, the duration of these symptoms varied from one to forty years. The youngest patient was 17 and the

oldest 78, with an average of 51 years; females predominated, in a ratio of 5 to 1.

It is not the size of the tumor which causes the most distress but its location. A small adenoma which will slip up and down under the sternum directly in front of the trachea will cause much more discomfort than an enormous intrathoracic tumor which has room to enlarge without causing pressure on the trachea or on the vessels of the neck. The average amount of tissue removed was 164 Gm., the largest tumor weighing 590 Gm. (case 2 [not described], figs. 2 and 3). One of these patients, with an intrathoracic tumor on the right, had definite cardiospasm for which dilation had been done repeatedly. Roentgenograms

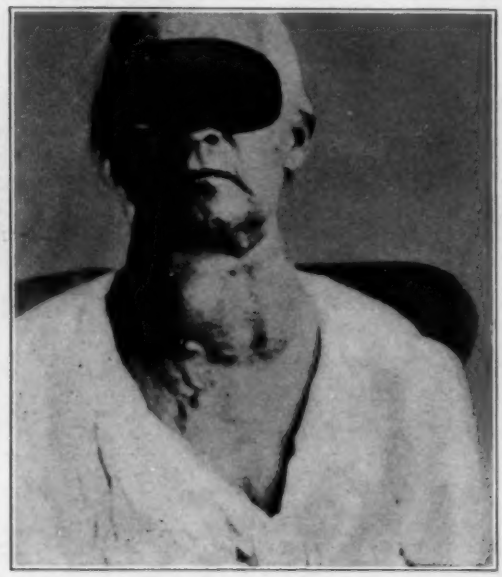

Fig. 2.—Patient in case 2 (not described in text).

of the distal part of the dilated esophagus had not included this intrathoracic tumor, and not until the tumor was removed did the cardiospasm subside.

Interference with swallowing was a very minor complaint in this series.

Laryngeal displacement and involvement of the vocal cords occurred in 13 patients, or 7 per cent, 3 of whom had been operated on previously and stated that changes in the voice followed operation. There were also 10 patients with involvement of the cords who had not had previous operations and undoubtedly the lesion of the vocal cords was due to stretching of the recurrent laryngeal nerve either by displacement of

the large vessels in the upper part of the thorax or by displacement of the larynx due to the tumor mass.

DIAGNOSIS

The diagnosis of intrathoracic and substernal goiters should not be difficult. From the history, the general appearance of the patient, the enlarged vessels, the husky voice, the cyanosis, the position of the larynx and trachea to palpation, the inability to palpate the lower poles of the gland and finally the fluoroscopic and roentgen evidence, one should be able to differentiate these goiters from aneurysm, lymphosarcoma, metastatic growth, lipoma and intrathoracic dermoids.

As is illustrated by case 1, a roentgenogram taken before operation may save the patient either one or two operations.

CASE 3.—Mrs. W. J. N., aged 50, was first seen on Sept. 25, 1939, on account of palpitation due to an enlarged thyroid. She had been operated on in 1919

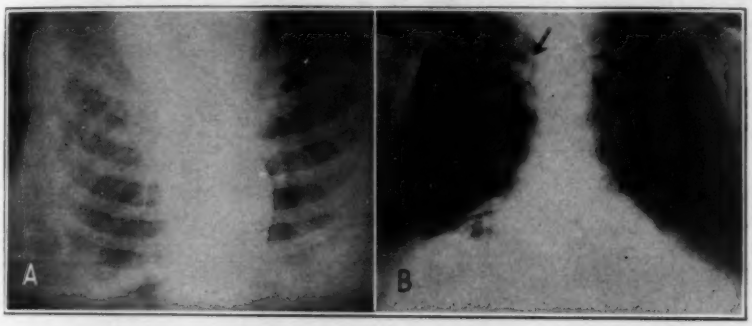

Fig. 3.—Roentgenograms taken in case 2 (not reported). The amount of tissue removed was 590 Gm. Roentgenogram *B* shows the result of treatment and indicates the point at which the clavicle was separated from the sternum.

for a large nodular goiter. This started to recur a year later, and in 1932 she was reoperated on. She had had no signs of pressure since her last operation, but her voice had been husky. Her history was otherwise irrelevant.

Examination showed that the left recurrent laryngeal nerve was paralyzed.

Roentgen examination showed a mass in the mediastinum extending down to the level of the sixth thoracic vertebra (fig. 4).

The patient was operated on Jan. 15, 1940, and the tumor was removed without injuring the right recurrent laryngeal nerve. Recovery was uneventful.

Again, this tumor was not suspected until a roentgenogram was taken shortly before the patient registered at the clinic.

OPERATIVE METHODS

Before operation, all the patients are carefully examined by a cardiologist and an internist and kept for from two days to weeks, preparing for surgical removal of the tumor.

My anesthesia for years for all goiters has been induced by injection of a local anesthetic agent into the skin and muscles, followed with ethylene. The usual collar incision is used. Twice in this series we have had to separate the clavicle from the sternum (case 2, fig. 3*B*) before being able to remove the tumor, and once it was necessary to perform a tracheotomy for compression of the trachea—during operation. The opening in the trachea was closed immediately after the

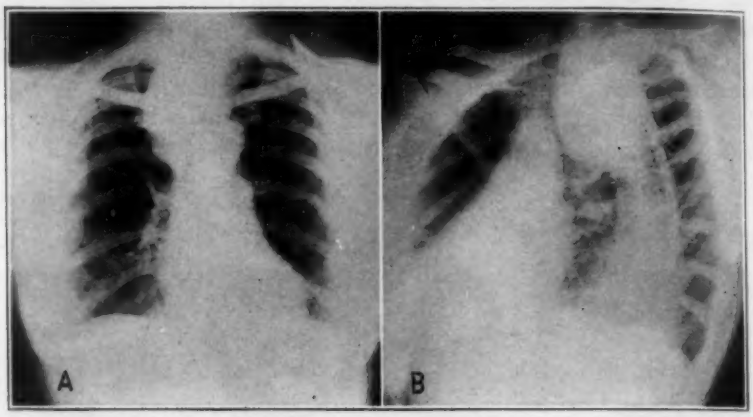

Fig. 4.—Roentgenograms taken in case 3. *A*, anteroposterior view; *B*, lateral view.

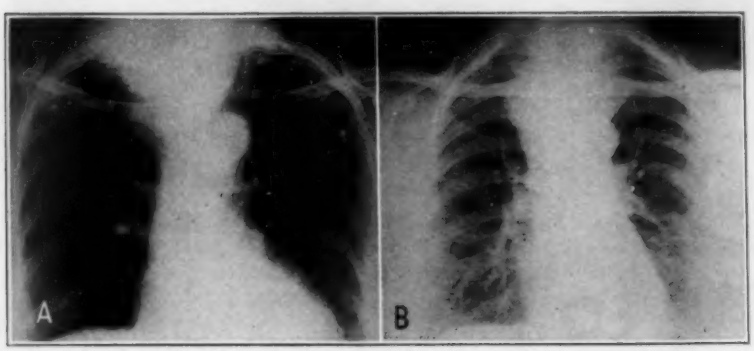

Fig. 5.—*A*, substernal goiter, showing the displaced trachea (case 4, not reported). *B*, bilateral substernal shadow (case 5, not reported).

obstruction was relieved. The tracheal rings have never been noticed to be softened from pressure or displacement with a benign growth, and in my experience only once, years ago, collapse of the trachea in a case of benign tumor occurred about twelve hours after operation. It was relieved by immediate tracheotomy; recovery of the patient followed.

Soft tracheal rings were noted only in cases of carcinoma of the thyroid with involvement of the trachea. In 3 cases of this series of intrathoracic and substernal goiters there was hemorrhage which from pressure required reopening of the wound and suturing of the gland or packing of the wound open. There were no bilateral nerve injuries, although unilateral paralysis has occurred. (I do not know the exact number of instances, as unfortunately no check was made postoperatively.) I have not attempted to obliterate the cavity from which the tumor was removed but have frequently left a gauze pack in the wound and gradually withdrawn it in from two to five days.

The mortality has been 0.05 + per cent for this group of patients; that is, there was 1 death, which occurred the day after operation from acute dilatation of the heart, and for the total number of thyroids operated on, 1,334, during this ten year period, there were 8 deaths, or 0.05 + per cent.

CONCLUSIONS

With care, injury to the laryngeal nerves may be avoided. Absolute hemostasis is necessary. Fluoroscopic study and roentgen plates are essential before secondary operations are undertaken.

ADENOMYOSARCOMA OF THE KIDNEY (WILMS TUMOR)

REPORT OF THREE CASES

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The large number of articles which have appeared during the past ten years on the subject of malignant renal tumors in children is evidence of the widespread interest in this subject. Not only does the urologist regard this subject with deep concern, but the pediatrician, the roentgenologist and the pathologist are equally interested. One of the results of this trend toward intensive clinical and pathologic study of malignant renal tumors on the part of the aforementioned specialists has been the uniform terminology now used in reporting the cases.

In a previous communication [1] I called attention to the fact that these tumors have certain characteristics which the ordinary renal tumors do not possess and that these may be enumerated as follows. 1. Although a few cases have been reported in which the tumor occurred in adults, the fact remains that it is essentially a disease of infancy and childhood. 2. As a rule it runs a silent and rapid course, as is evidenced by the fact that the tumor reaches a large size before medical aid is sought. 3. The histologic picture is unique and singularly characteristic. 4. The outcome is generally fatal. 5. A multiplicity of theories have been advanced from time to time regarding the pathogenesis.

The cause of the Wilms tumor, in common with that of other malignant tumors, is unknown. However, the consensus seems to be that it is congenital. In none of my cases was I able to obtain a definite history of trauma, although in 1 instance the mother thought the child had been injured.

Many theories have been advanced concerning the pathogenesis of this type of tumor, and it may be desirable to review some of them briefly here.

PATHOGENESIS OF WILMS TUMOR

Eberth [2] gave a very accurate description of a mixed tumor of the kidney. He called attention to the presence in such neoplasms of more

From the Children's Memorial Hospital.

1. Kretschmer, H. L.: J. Urol. **39**:250-275, 1938.
2. Eberth, C. J.: Virchows Arch. f. path. Anat. **55**:518, 1872.

than one type of tissue and attributed their origin to inclusions of the wolffian body. He attempted to account for the presence of striated muscle on the ground that the connective tissue of the wolffian body is rich in embryonal muscle cells. Later authors pointed out that the embryonal tissue Eberth referred to gives rise to nonstriated but not to striated muscle fibers.

Birch-Hirschfeld [3] expressed agreement with Eberth that these tumors have their origin in the wolffian body. He expressed the belief that such an origin would explain the intimate relation between the tumor and the kidney, without, however, a true blending between the renal substance and the tumor tissue. Later he wrote that the glandular tissue is primary, having its origin in the residual tubules of the wolffian body.

Busse [4a] and Muus [4b] advanced the hypothesis that mixed renal tumors originate from a segregated portion of the renal blastoma, which at some time during its fetal life proliferates and fails to develop normally. The various types of tissue present develop by a process of metaplasia.

Wilms [4c] pointed out that the wolffian body cannot be expected to produce the variety of tissues found in these growths and that they are mesodermal in origin. He assumed that their anlage is a fragment of the primitive undifferentiated mesodermal tissue of the type which in the course of normal development gives rise to the myotome, the sclerotome and the nephrotome.

Herzog and Lewis [5] stated the belief that these tumors owe their origin to an inclusion which is formed when the nephrotome is not cut off at the usual site but is cut off in such a manner that a portion of either the myotome or the sclerotome or both remains in connection with it.

Hinman and Kutzmann [6] called attention to the fact that opinion concerning these embryonic mixed tumors is far from uniform. They stated that it is possible that the simple tumors, or so-called sarcomas, may be explained by Birch-Hirschfeld's theory and the more complex types by Wilms's theory.

Dean and Pack [7] expressed the opinion that, as these tumors may vary markedly in the degree of differentiation of their component cells

3. Birch-Hirschfeld, F. V.: Centralbl. f. d. Krankh. d. Harn- u. Sex.-Org. **5**:97, 1894.

4. (*a*) Busse, O.: Virchows Arch. f. path. Anat. **157**:346 and 377, 1899. (*b*) Muus, N. R.: ibid. **155**:401-425, 1899. (*c*) Wilms, M.: Die Mischgeschwülste der Niere, Leipzig, Arthur Georgi, 1899.

5. Herzog, M., and Lewis, D.: Am. J. M. Sc. **119**:693-701, 1900.

6. Hinman, F., and Kutzmann, A. A.: Ann. Surg. **80**:569-590, 1924.

7. Dean, A., and Pack, G.: Embryonal Adenosarcoma of Kidney, J. A. M. A. **98**:10-17 (Jan. 2) 1932.

and in the number of tissues represented, it is evident that they originate at different embryonic developmental periods. The renal blastoma, or nephrotome, is the predominant contributing structure.

Geschickter and Widenhorn [8a] stated that the earlier theories of pathogenesis, relating the Wilms tumor to the wolffian body or to aberrant rests from the sclerotome and myotome, have been superseded by data relating these tumors to embryonic nephrogenic tissue. They stated:

> Approximately two-thirds of all Wilms tumors contain only those microscopic elements of spindle cells and early tubule formation which can be found in the normal embryonic kidney or in the zone of development just beneath the capsule of the kidney in normal infants a few months after birth. The majority of these tumors, therefore, are of the normal developmental processes occurring in the growth bones of the renal cortex in late fetal life or in the first few months after birth.
>
> The occurrence of cartilage, bone, or muscle in approximately one-third of these new growths is not strange when we consider that the more undifferentiated mesenchymal spindle cells found in the normal nephrogenic tissue in the process of development may retain the multiple potentiality for the elaboration of all of the normal mesenchymal derivatives.

Ewing [8b] called attention to the fact that "the interpretation of the origin of renal mixed tumors has passed through several phases and covered all apparent possibilities. An origin from an aberrant sex cell has been deemed necessary by Ribbert, who interpreted some of the epithelial rosettes as neuro-epithelium, and who emphasizes the presence of all three germ layers."

I shall present 3 cases of Wilms tumor observed at the Children's Memorial Hospital since the last series of cases was published.[1]

REPORT OF CASES

CASE 1.—E. S., a white boy aged 1 year and 8 months, was admitted to the Children's Memorial Hospital Dec. 12, 1937.

Previous History.—The previous history was irrelevant.

Complaints on Admission.—There had been gradual enlargement of the abdomen and loss of weight for two months, restlessness and irritability for two weeks, diarrhea for the past few days, swelling of the legs for one day and a slight cough for several days. Three days previously the child had had an attack of vomiting; he was always constipated. The mother said that there had been some frequency of urination, but she was very indefinite in her statements.

Physical Examination.—The child was acutely uncomfortable, with grunting, embarrassed respiration. The head, neck and heart were normal. A few rales were heard at the base of the left lung. The abdomen was enormously distended;

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8. (*a*) Geschickter, C. F., and Widenhorn, H.: Am. J. Cancer **22**:620-658, 1934. (*b*) Ewing, J.: Neoplastic Diseases, ed. 3, Philadelphia, W. B. Saunders Company, 1934, p. 797.

prominent, engorged blood vessels were observed over the front and side of the abdomen (fig. 1). The abdomen was very tense and flat on percussion. There was a large, hard mass in the left flank, which extended to the pubic area. There was marked protrusion of the umbilicus.

Rectal Examination: The lower border of the mass was felt; there were definite signs of fluid in the peritoneal cavity.

Blood Pressure: The blood pressure was 80 systolic and 68 diastolic.

Blood.—Examination of the blood showed: red blood cells, 3,100,000 per cubic millimeter; white blood cells, 22,500 per cubic millimeter; hemoglobin, 62 per cent;

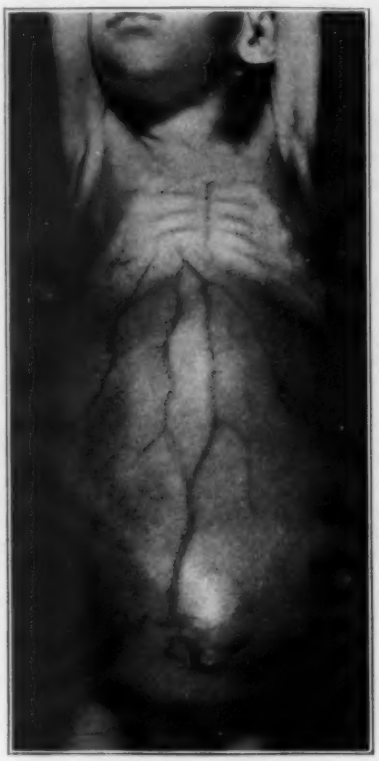

Fig. 1 (case 1).—Enormous distention of superficial veins of the abdomen and of the lower part of the chest. Note the marked protrusion of the umbilicus.

polymorphonuclear neutrophils, 70 per cent; lymphocytes, 27 per cent; eosinophils, 1 per cent, and basophils, 3 per cent. The Wassermann and Kahn reactions were negative. The value for nonprotein nitrogen was 38.1 mg. and that for urea nitrogen 22.2 mg. per hundred cubic centimeters.

Urine.—Repeated examinations of the urine gave negative results.

Roentgen Examination.—The chest showed no metastases. The diaphragm was elevated. A large homogeneous mass nearly filled the abdomen. There was lateral and upward displacement of intestinal gas shadows (fig. 2 *A*).

Intravenous pyelograms showed dilatation of the ureter, pelvis and calices of the right kidney (fig. 2 *B*). There was only partial visualization of the slightly dilated calices on the left side.

Abdominal Paracentesis.—On December 13 thick, bloody fluid and a few pieces of tumor tissue were obtained. Histologic examination (Dr. W. G. Hibbs) of these pieces showed the presence of Wilms tumor.

Treatment and Course.—A course of high voltage roentgen therapy was recommended and carried out. The patient received twelve treatments, consisting of 2,436 r. After the treatment was begun there was some recession in the size of the abdomen, but this was only temporary, and the abdomen gradually increased in size. The child was discharged from the hospital on Feb. 28 1938. He died at home on March 21.

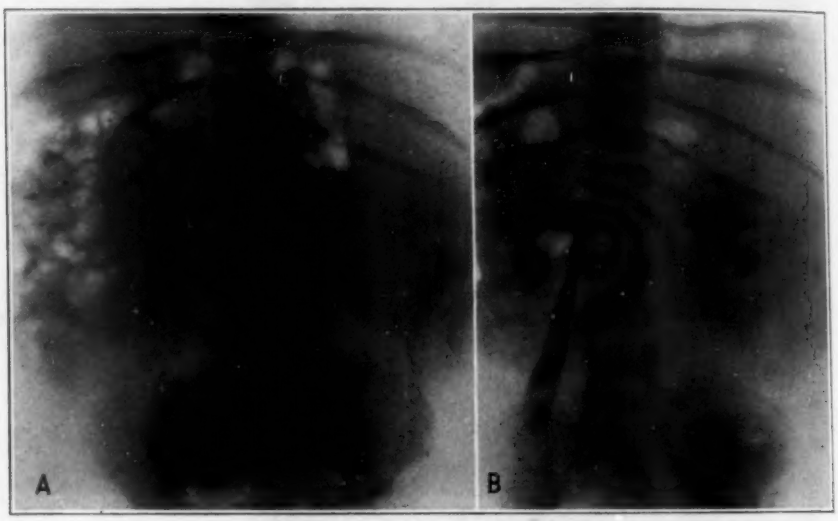

Fig. 2 (case 1).—*A*, lateral and upward displacement of the intestinal gas shadows. *B*, dilatation of the ureter and calices on the right side, due to pressure by the tumor. A small collection of dye is seen on the left side.

Comment.—This case illustrates the fact that not all Wilms tumors show a marked reduction in size after high voltage roentgen treatment.

CASE 2.—K. C., a white boy aged 2½ years, was admitted to the Children's Memorial Hospital Aug. 17, 1938.

Previous History.—The history was unimportant except for chickenpox in 1937.

Complaints on Admission.—The mother stated that the child had had some abdominal pain for the past twenty-four hours. She also stated that she had felt a mass on the right side; it had never been noticed prior to this time. On the previous day she had noted for the first time a moderate amount of blood in the urine. All subsequent specimens had shown gross blood.

Physical Examination.—The boy was well developed and well nourished. The head and neck were normal except for injection and slight bulging of the left ear drum. The heart and lungs were normal. Examination of the abdomen showed

a large, rounded, smooth, hard, nontender mass on the right side, extending to the left of the midline. The mass filled the entire right half of the abdomen. There was no rigidity. The liver and spleen were palpable. The external genitalia were normal. The lower border of the tumor was easily felt with the finger on rectal examination.

Blood Pressure: The blood pressure was 150 systolic and 95 diastolic.

Blood.—Examination of the blood showed: red blood cells, 5,450,000 per cubic millimeter; white blood cells, 6,000 per cubic millimeter; hemoglobin, 80 per cent; polymorphonuclear neutrophils, 54 per cent; lymphocytes, 42 per cent;

Fig. 3 (case 2).—There is no visualization on the side occupied by the tumor. The opposite pyelogram is normal.

mononuclears, 2 per cent; eosinophils, 1 per cent, and basophils, 1 per cent. The Wassermann and Kahn reactions were negative. The value for nonprotein nitrogen was 38.1 mg. per hundred cubic centimeters.

Urine.—The reaction was acid; albumin was present; there was no sugar; blood was present; there were many red blood cells and occasional white blood cells, but there were no casts. Repeated examinations of specimens of urine on three occasions revealed blood and red blood cells.

Roentgen Examination.—The chest showed no evidence of metastases. There were no signs of calculi in the urinary tract. An intravenous pyelogram showed the left side to be normal. There was no visualization of the dye on the right side (fig. 3). A large shadow in the soft parts, suggestive of tumor, was seen.

The diagnosis was Wilms tumor of the right kidney. A course of high voltage roentgen therapy was instituted, and a total of 3,192 r was given. There was no diminution in the size of the tumor. Operation was advised.

Operation.—On September 22, with the child under ether anesthesia, the usual oblique lumbar incision was made on the right side, and a nephrectomy was performed.

Histologic Diagnosis.—The diagnosis was Wilms tumor (Dr. W. G. Hibbs).

Postoperative Course.—The course was uneventful, and the child was discharged from the hospital on October 14. Postoperative therapy was advised.

Subsequent Course.—The child died at home very suddenly on Aug. 7, 1939. He came in from play complaining of being tired, went to bed and died in one hour.

CASE 3.—M. W., a white boy aged 7 years, was admitted to the Children's Memorial Hospital Aug. 14, 1939.

Previous History.—The history was unimportant except for an attack of lobar pneumonia in March 1937, followed by complete recovery.

Complaints on Admission.—There was a large mass in the abdomen. The mother stated that the child had apparently been well; he had not complained. About a week previously she had noticed that the right side of the abdomen was larger than usual and that the umbilicus was more prominent. There were no complaints referable to the urinary tract and no history of hematuria. The child slept well, played heartily and had a good appetite.

Physical Examination.—The boy was well developed and well nourished, with a sallow complexion and a fine texture of the skin. The head and neck were normal except for the presence of some enlarged, nontender cervical glands. The heart and lungs were normal. The diaphragm was high, especially on the right side. A mass in the right upper quadrant of the abdomen, hard but not tender, extending forward from the region of the kidney to the outer edge of the rectus muscle, was present. The lower edge of the tumor was at, or slightly below, the level of the anterior superior spine of the ilium. The upper edge of this mass, the surface of which was smooth, was separate and distinct from the edge of the liver. The liver was enlarged and extended about 3 fingerbreadths below the costal margin. The veins over the right side of the abdomen and the lower part of the chest were prominent (fig. 4).[5]

Blood Pressure: The blood pressure was 120 systolic and 90 diastolic.

Blood.—Examination of the blood showed: red blood cells, 4,100,000 per cubic millimeter; white blood cells, 6,900 per cubic millimeter; hemoglobin, 81 per cent. On August 15 the value for nonprotein nitrogen was 44.4 mg.; that for creatinine, 1.5, and that for uric acid, 3.8 mg., per hundred cubic centimeters. On September 20 the values were: nonprotein nitrogen, 28.2 mg.; creatinine, 1.1 mg., and urea nitrogen, 12.2 mg.

Urine.—The reaction was acid; the specific gravity was 1.024; there was a trace of albumin but no sugar. An occasional white blood cell was seen. Otherwise the urine was normal. Subsequent examinations of the urine during the entire stay in the hospital gave negative results except for one specimen (September 27), which was loaded with pus.

Roentgen Examination.—A plain film of the abdomen showed no stone in the urinary tract. A large shadow in the soft parts was seen, nearly filling the abdomen. Roentgen study of the chest (August 15) showed the leaves of the

diaphragm to be high. On August 31 a metastatic area in the lung was observed, measuring 2 by 2.5 cm. On September 6, the density appeared slightly larger; the patient had received two roentgen treatments to the chest. On September 15, anteroposterior and lateral views failed to show the oval dense shadow noted previously in the base of the right lung. On September 25 there was no roentgen evidence of a pulmonary lesion or of fluid in either pleural cavity.

On August 16, intravenous pyelograms showed normal conditions on the left and no evidence of the visualizing mediums on the right side. A very large shadow was seen in the soft parts.

Fig. 4 (case 3).—Enormous distention of the superficial veins extending from the sternum to the symphysis pubis.

Cystoscopic study revealed that the bladder and the ureteral orifices were normal. The retrograde pyelogram showed a filling defect compatible with tumor of the right kidney (fig. 5).

Examination of the Abdomen.—On August 24 there was definite enlargement. The veins were more prominent over the lower part of the thorax and the upper part of the abdomen than they had been at the previous examination. There was unmistakable ascites. The umbilicus was very large and protruding.

Diagnosis.—The diagnosis was Wilms tumor. High voltage roentgen therapy was advised. The patient was given 2,000 r.

Abdominal Paracentesis.—On August 20, 1,300 cc. of fluid was removed. Examination for tumor cells gave negative results.

Course.—On August 29 there was edema of the scrotum. The veins of the upper part of the abdomen and the lower part of the chest were markedly increased in size. The liver was enlarged, hard, irregular and nodular.

On September 10 ascites was noted to be increasing rapidly again. Edema over the chest was less marked. There had been edema of the left leg during the last two days. By abdominal paracentesis (September 12) 2,700 cc. of slightly

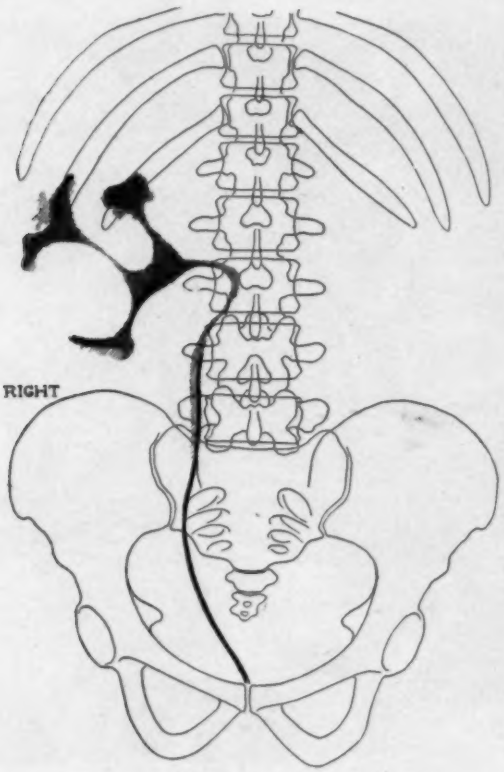

Fig. 5 (case 3).—Schematic representation of a retrograde pyelogram, showing a filling defect compatible with tumor.

cloudy straw-colored fluid was withdrawn. Culture of the fluid showed Staphylococcus albus.

The patient died on September 29. Postmortem roentgen study of the lungs by Dr. Anspach again failed to show the metastases in the right lung noted on September 6.

In spite of the seeming improvement and the disappearance of the nodular shadows in the roentgen films, the lungs on postmortem examination were riddled with active metastatic nodules.

Autopsy (Dr. W. G. Hibbs).—There were embryoma of the right kidney, with direct invasion of the inferior vena cava, adrenal vein, renal vein and right auricle; thrombosis of the left common iliac, hypogastric external iliac and saphenous veins; thrombosis of the right common iliac vein; fibrous adhesions between the tumor, gallbladder, liver and duodenum; duodenal obstruction; metastases in the liver, the lung and the retroperitoneal tissue; congestion of the liver; ascites; edema of the left lower extremity, and right pleural adhesions (fig. 6).

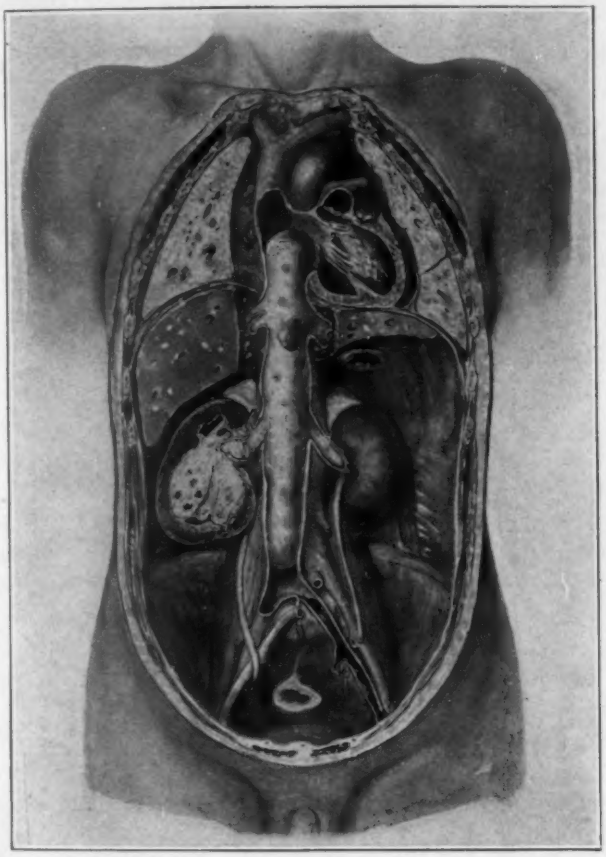

Fig. 6 (case 3).—Tumor in the right kidney, with a tumor thrombus in the adrenal vein, both renal veins and vena cava. The tumor thrombus extends into the right auricle.

Comment.—There are three interesting and outstanding facts in this case. 1. After roentgen treatment of the chest, the metastatic nodule seen in the films made September 6 was not demonstrable by the roentgenogram. Roentgen examination of the lungs prior to autopsy revealed no abnormality, yet autopsy showed that the lungs were riddled with metastases. This introduces the question whether a "nega-

tive" film always means absence of metastases to the lung. 2. Roentgen therapy failed to cause a reduction in the size of the tumor. 3. There was extension of the tumor from the kidney into the right auricle.

AGE

The Wilms tumor occurs with great frequency in infants and young children. In two thirds of my cases the patients were under 4 years of age.

Schaffer [9] reported a case in which the tumor occurred in the single kidney of a deformed fetus, and Lubarsch [10] described 4 cases of its occurrence in fetuses and newborn infants. Cases have been reported of its occurrence in adults, but they are very rare.

SEX

The sex incidence is of little aid in the diagnosis. In my previous studies [11] 18 patients were males and 6 were females. In the 3 cases that form the basis of this paper all the patients were boys. It would appear, therefore, that boys are more frequently afflicted than girls (77.77 per cent).

GROSS PATHOLOGIC PICTURE

The Wilms tumor is predominately unilateral. Bilateral tumors have been reported but they are uncommon. I have observed 2 such growths. The tumor varies greatly in size. The smallest tumor that I have seen weighed 235 Gm. The growth may nearly fill the abdomen and extend into the pelvis so that it can be felt on rectal examination. This occurred in 2 of the 3 cases reported in this paper. There may be displacement of viscera. The tumor may take its origin from either the upper or the lower pole or in the middle of the kidney. It is encapsulated; it is globular or oval, and it often appears lobulated. The surface is generally smooth, although a nodule may protrude above it. The kidney is separated from the tumor by a sharp line of demarcation (fig. 7). The kidney is compressed by the growth and suffers from pressure atrophy. The pelvis also is compressed except in the rare instances in which the tumor seems to grow around the pelvis. In my experience the tumor is solid. In none of my cases did it have the appearance of a polycystic kidney, although this has been mentioned in the literature.

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9. Schaffer, cited by Ewing.[8b]

10. Lubarsch, cited by MacKenzie, in Cabot, H.: Modern Urology in Original Contributions by American Authors, ed. 3, Philadelphia, Lea & Febiger, 1936, vol. 2, p. 723.

11. Kretschmer, H. L., and Hibbs, W. G.: Surg., Gynec. & Obst. **52**:1-24, 1931.

The tumor may invade the renal vein. In 1 of my cases (case 3) it invaded the renal vein and the vena cava and extended into the right auricle of the heart. Invasion of the heart by a tumor thrombus is very rare (fig. 7). In Merkel's [12] case a tumor thrombus extended from the invaded vena cava into the heart.

The cut surface is generally firm and lobulated and varies in color. Dark areas are often present due to hemorrhage within the tumor. In some instances the tumor presents a lobulated appearance due to connective tissue.

Fig. 7 (case 2).—Line of demarcation between the tumor and the kidney. Note the dark area in the tumor, due to hemorrhage.

MICROSCOPIC PATHOLOGIC PICTURE

In a previous publication [11] Hibbs and I stated:

> The embryonal structure of these tumors is their most distinguishing feature with a variety of tissue of abortive renal elements. The types of cells and amount vary in different tumors. They are usually myxomatous tissue composed of masses of polymorphous nucleated cells in which are imbedded gland or duct like figures resembling uriniferous tubules which may be sparse or abundant. These embryonic tubules in a heterogeneous matrix are the most conspicuous features. . . . In addition there are epithelial and connective tissue elements. The connective tissue elements consist of loose stroma, undifferentiated round cells, striated and nonstriated muscle fibers.

12. Merkel: Beitr. z. path. Anat. u. z. allg. Path. **24**:475, 1898.

Cartilage and bone cells may be present in some of these tumors, but they are rare and I have never seen them.

SYMPTOMS

It is a well recognized fact that this sort of tumor runs a relatively silent course. As can be readily understood, this is most unfortunate for the patient, since in many cases treatment is sought too late for surgical relief, as was instanced in 2 of the 3 cases reported in this paper. Another drawback is the fact that symptoms referable to the urinary tract are absent, with the possible exception of the rare cases in which hematuria is present. Likewise, pain is a relatively uncommon symptom and occurs late in the course of the disease. Anemia and loss of weight are late manifestations; hence, when the child is brought to the physician because of these symptoms the condition is far advanced. Pressure symptoms, such as nausea, vomiting, constipation and shortness of breath, are also late occurrences.

What is most unfortunate in these cases is that the symptom that most frequently brings the child to the physician is the presence of an abdominal tumor, accidentally noted by the mother or nursemaid.

A palpable tumor was noted in each of the 3 cases reported in this paper. The enlargement was always progressive and painless. The growth varied in size within more or less wide limits, that is, from a small tumor which was just palpable to one which filled or nearly filled the abdomen. In 2 of the cases the tumor extended into the pelvis, so that its lower border was felt with the finger in the rectum. It is rarely if ever, painful on palpation, and the consistency is hard. The surface may be smooth and nodular. In the larger tumors there may be upward displacement of the diaphragm, and in several of my cases the intestines were displaced to the lateral border of the abdomen (fig. 2).

DIAGNOSIS

As a rule the diagnosis presents no difficult problem. The presence of an abdominal tumor which has rapidly increased in size and is hard, sometimes nodular and nearly always painless, coupled with the fact that the commonest abdominal tumor in children is the Wilms tumor, should lead to a tentative diagnosis of that tumor in the case of every child with an abdominal growth.

The diagnosis should be based on the results of a complete urologic study in every case. The plain roentgen examination often reveals a large shadow in the soft parts that in general conforms to the size and shape of the abdominal tumor. But its presence is not pathognomonic of a Wilms tumor, since other retroperitoneal tumors, and occasionally a large hydronephrosis, may cause a similar shadow.

The diagnosis is further strengthened by changes in the pyelogram that are compatible with tumor. In a previous publication, however, attention was called to the fact that in very rare instances the tumor in its growth produces no changes in the pelvis and that therefore the pyelogram may be normal, a fact that should not be overlooked.

In every case in which a tentative diagnosis of Wilms tumor is made, a plain roentgenogram of the chest is taken to rule out the possibility of metastasis, and a plain film of the abdomen is made to rule out stone in the urinary tract. A shadow on the affected side is generally present, and this concurs more or less closely with the size and outline of the tumor. It would be well to bear in mind that a large shadow in the soft parts is not necessarily pathognomonic of a Wilms tumor but may be due to hydronephrosis, neuroblastoma or some other retroperitoneal tumor.

The next step in examination consists of obtaining a set of intravenous urograms. Occasionally there may be complete failure to visualize the renal pelvis on the affected side although the opposite pelvis is shown as normal. But, on the other hand, the pyelogram is frequently most dependable, since it shows a filling defect compatible with tumor. In case the intravenous pyelograms do not yield the desired information, a retrograde pyelogram should be made. Cystoscopic examination, catheterization and functional tests are carried out before removal of the tumor is undertaken.

Failure to visualize the pelvis does not always mean tumor and hence must be checked with a retrograde pyelogram. In 1 case in which a tentative diagnosis of Wilms tumor was made and in which there was no visualization of the pelvis, a retrograde pyelogram was not made. At operation a large hydronephrosis was found.

It is necessary, of course, to rule out other retroperitoneal tumors, such as neuroblastoma, sarcoma and lipoma. At times it may be necessary to differentiate enlargements of the spleen, tumors of the ovary and cysts of the omentum. As a rule these offer no special problem after a complete urologic study has been carried out.

TREATMENT

A good many differences of opinion still exist as regards the best form of treatment. McNeill and Chilko,[13] in a survey of 383 cases reported in the literature or observed personally, found that six types of treatment have been followed: (1) nephrectomy alone; (2) the use of serum in conjunction with nephrectomy, Coley having reported a good result from this method; (3) roentgen therapy to reduce the size of the tumor and kill the embryonal cells, followed by nephrectomy; (4)

13. McNeill, W. H., Jr., and Chilko, A. J.: J. Urol. **39**:287-302, 1938.

roentgen therapy followed by nephrectomy and by another course of roentgen treatment; (5) nephrectomy followed by postoperative roentgen treatment in order to destroy any residual malignant embryonal cells, and (6) roentgen treatment alone. They reported the case of 1 patient alive and well three years after irradiation.

Ladd [14] suggested that operation be carried out without delay once the diagnosis has been established.

At present the routine followed by my associates and me is to give the patient a course of high voltage roentgen therapy followed by nephrectomy, after which another course of high voltage roentgen therapy is carried out.

In my experience, not all Wilms tumors are radiosensitive. When the growth is radiosensitive and shows a marked reduction in size, it certainly simplifies nephrectomy.

With the diminution in size of the tumor, corresponding changes are observed in the pyelogram. Attention was called to this phenomenon in a previous publication.[1]

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14. Ladd, W. E.: Ann. Surg. **108**:885-902, 1938.

FEVER AS INITIAL SYMPTOM OF HYPERNEPHROID TUMOR OF THE KIDNEY

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The purpose of this brief paper is to report a case of renal tumor in which the classic triad of hematuria, pain and a palpable abdominal mass was absent. The only clinical manifestation was an obscure febrile state of one year's duration, accompanied with nausea, vomiting and irregular uterine bleeding from multiple fibroids.

FEVER WITH RENAL NEOPLASIA

The first reference to fever associated with renal neoplasia was made by Israel [1] in 1896. In the case reported by him a man 43 years of age suffered from a hectic remittent fever for several months. At operation a right hypernephroid tumor of the kidney was found. The fever promptly disappeared after removal of the kidney.

In 1911, Israel [2] again commented on the importance of fever as a diagnostic symptom of renal tumor. It was present as part of the picture in 18.3 per cent of the cases that he reported. Concerning the cause of fever he stated: "One does not know what the fever-exciting noxious agent is." Degeneration resulting from bacterial action, which readily plays a part in the causation of gastric, intestinal and uterine tumors, is out of the question with these wholly aseptic tumors of the kidney and adrenal. The cause of the fever must be looked for in the rapid growth of tumor cells or in the destruction of normal tissue. Israel referred to a pyrogenic substance that is elaborated by tumor cells as another possible source of the fever.

Voelcker [3] suggested that the fever in these cases might be the first recognizable symptom of the disease. He thought that the febrile state might be due to the "absorption of albumin bodies produced by the process of involution."

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1. Israel, J.: Ueber einige neue Erfahrungen dem Gebiete der Nierenchirurgie, Deutsche med. Wchnschr. **22**:345, 1896.

2. Israel, J.: Fieber bei malignen Nieren- und Nebennierentumoren, Zentralbl. f. Chir. **41**:10, 1911.

3. Voelcker, T.: Die Neubildungen der Niere, in Kraus, F., and Brugsch, T.: Spezielle Pathologie und Therapie inneren Krankheiten, Berlin, Urban & Schwarzenberg, 1920, vol. 7, p. 653.

Warburg [4] has shown that tumor cells have a metabolism of their own which differs from that of normal cells. This difference in metabolism between normal and neoplastic cells may cause the change in body economy that produces the variation in temperature.

While the exact cause of the febrile state in cases of renal neoplasia has never been definitely settled, it is believed to be anaphylactic. The fever associated with rapid growth and great size of the renal tumor may be caused by toxic absorption of the products of metabolism of the neoplastic tissues. Foreign proteins are elaborated either by the tumor growth or by central necrosis of the malignant tissue. This material is disseminated by the blood stream. It acts on the thermal centers as a foreign protein, causing anaphylactic elevation of temperature. The fever subsides after the tumor has been removed. When the temperature does not subside after nephrectomy, distant metastases may be suspected.

Fever as an isolated symptom suggesting renal tumor has not been frequently reported in the literature. It may occur irrespective of complicating pyelonephritis. This occurred in the case reported by Nicholson.[5] The patient was a woman 38 years of age who had had an unexplained continuous fever for two years. Even after the most searching and extensive examinations the cause of the fever remained undiagnosed. A renal carcinoma was found at autopsy. Ljunggren [6] (who in 1930 published a clinical and prognostic study of Grawitz' tumors [7]) reported the case of a woman, 52 years of age, with an undiagnosed fever of six months' duration. Urologic investigation revealed a left kidney with the typical characteristics of renal tumor. The patient's temperature became normal and remained so after nephrectomy. Creevy [8] reported 2 interesting cases in which fever played an important part in the clinical picture. The first was that of a patient whose temperature varied between 100 and 102 F. for two months. A diagnosis of infected hydronephrosis was made, and the elevation of temperature was explained on that basis. At operation an extensive renal carcinoma was found. The patient remained free from

4. Warburg, O.: Ueber den Stoffwechsel von Tumoren im Körper, Klin. Wchnschr. **5**:829, 1926.

5. Nicholson, D.: Fever with Renal Carcinoma, Arch. Path. **3**:393 (March) 1927.

6. Ljunggren, E.: Case of Renal Tumor with Fever as the Only Symptom, Brit. J. Urol. **4**:249, 1932.

7. Ljunggren, E.: Studien über Klinik und Prognose der Grawitzchen Nierentumoren, Acta chir. Scandinav. (supp. 16) **66**:1, 1930.

8. Creevy, C. D.: Pyrexia in Malignant Nephroma, J. A. M. A. **92**:1256 (April 13) 1929; Confusing Clinical Manifestations of Malignant Renal Neoplasms, Arch. Int. Med. **55**:895 (June) 1935.

fever after the operation. It is quite possible that the temperature was due to the renal neoplasia.

Creevy's second case was that of a woman 39 years of age with a low grade fever of several months' duration. She was thoroughly studied, and repeated agglutination tests were made, but no definite information was obtained. She was suspected of having a Brucella abortus infection. At autopsy a large necrotic hypernephroma was found. There was no evidence of metastasis.

Castano and Resolia reported a case in which an intermittent fever was the initial symptom of renal tumor. In this case the differential diagnosis included pain, nephric abscess and hydatid cyst of the liver.

In my series of 66 cases of renal neoplasm, fever was present as a complication in 37. In 28 cases the patients were afebrile; in 1 case fever was the only manifestation.

REPORT OF A CASE

Mrs. C. D., a white married woman aged 47 years, complained of weakness, fever, gastrointestinal distress and irregular menstruation. She was admitted to the service of Dr. R. J. Frodey, chief of the gynecologic division, for study and investigation.

The patient had been in her usual good health until approximately one year prior to her admission to the hospital, at which time she began to complain of general malaise and "spells of weakness" accompanied with nausea but no vomiting. Other symptoms, noted at the same time, were moderate dyspnea on exertion and frequent night sweats. The aforementioned symptoms continued, and approximately three months later, four months prior to admission, she began to feel nauseated after meals and frequently would vomit food just eaten. Two months prior to admission the nausea, vomiting and weak spells became more frequent and more severe.

There had been a daily rise in temperature from 99 to 102 F. for the past year. One month prior to admission she had been studied by the staff at the Tuberculosis Hospital. They were unable to demonstrate any active pulmonary lesion after exhaustive studies. Roentgen and physical examinations revealed no abnormality. At the time of the study she had leukocytosis, the white blood cell count being 17,750 per cubic millimeter, with 82 per cent polymorphonuclears. For this reason, Dr. L. H. Heatherington suggested further investigation as to some other source of infection.

For the past three years her menses had been irregular in onset, in duration and in amount of flow. The periods had been coming every two or three weeks, and during the past three months she had noticed that the amount of flow had definitely decreased. During the past year she had lost 18 pounds (8.2 Kg.) in weight. She had not had any cough, pain in the chest or hemoptysis. She had frequently noticed palpitation after exertion. There had been no symptoms referable to the urinary tract. There was no pain, burning, frequency of urination, dysuria, nocturia or hematuria. The past medical history, family history and social history were not contributory.

Physical Examination.—The patient was somewhat obese. She was nervous. She was resting in bed. The skin was warm and dry. There was no cyanosis, edema or dyspnea.

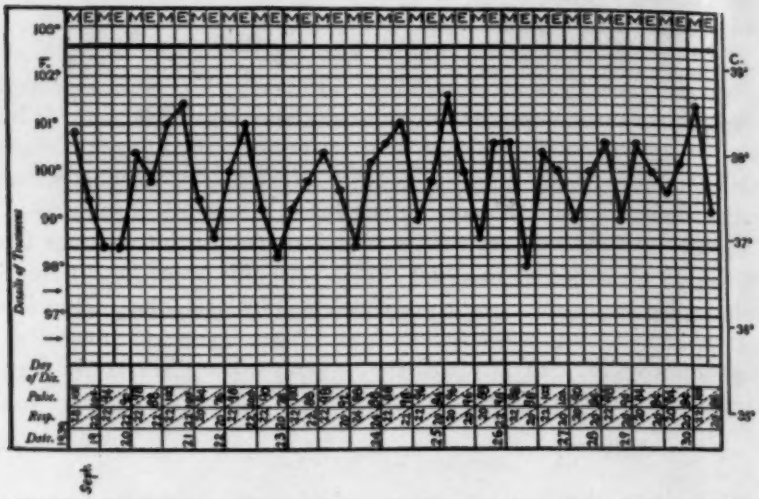

Fig. 1.—Record of the patient from September 19 to 30. On admission the value for hemoglobin was 60 per cent. The red blood cell count was 3,740,000 and the white blood cell count 8,950 per cubic millimeter. On September 30 a transfusion of 500 cc. of citrated blood was given.

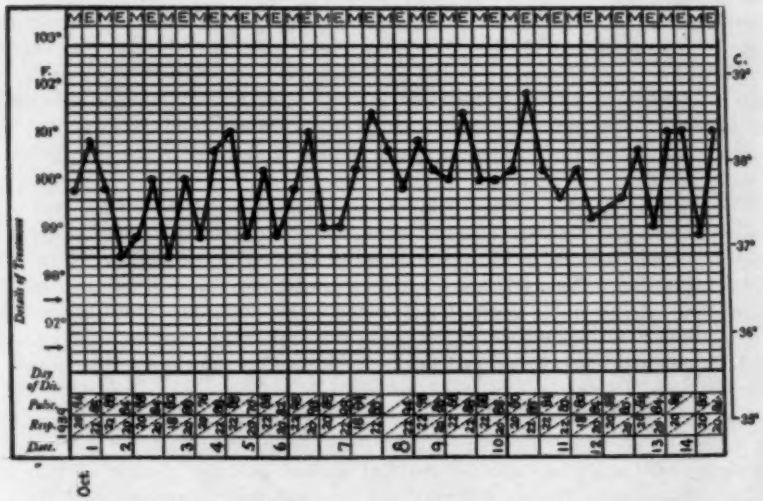

Fig. 2.—Record of the patient from October 1 to 14. On October 4 there were 4,200,000 red blood cells per cubic millimeter, with 78 per cent hemoglobin. On October 5 a transfusion of 500 cc. of citrated blood was given.

The only positive findings were a small firm, nontender mass just above and to the right of the symphysis pubis and a healed low midline incision. The chest was clear. The heart was essentially normal. The blood pressure was 140 systolic and 85 diastolic. The temperature was 100.8 F.; the pulse rate was 108, and the respiratory rate was 28.

Laboratory Studies.—The following data were obtained. The urine was normal on repeated examinations.

The phthaleins ranged between 50 and 70 per cent.

A blood count on September 19 showed: red blood cells, 3,740,000 per cubic millimeter; hemoglobin, 60 per cent, and white blood cells, 8,950 per cubic millimeter. Another count, on October 4, showed: red blood cells, 4,200,000 per cubic millimeter, and hemoglobin, 78 per cent.

An Ewald test meal on September 26 revealed the value for free hydrochloric acid to be 14, and that for total acid, 30. The blood was normal.

The feces were negative for blood on three occasions.

Macroscopic serologic tests of the blood for typhoid and undulant fever gave negative results.

Roentgen Studies.—On September 20, roentgen examination after a barium sulfate enema gave essentially negative results except for a soft tissue mass on the right side, not connected with the colon. The right kidney was enlarged.

On October 10 the stomach and duodenum were essentially normal.

Transfusions.—The patient's blood was of group 2 (Moss). The following transfusions were given:

September 30 500 cc. of citrated blood
October 5 500 cc. of citrated blood
October 16 500 cc. of citrated blood

Further Roentgen Studies.—September 25: Investigation up to this point as to nausea, vomiting and the febrile state had not revealed any positive findings. A plain plate of the abdomen at the time of the gastrointestinal studies revealed the right kidney to be somewhat larger than the left, and a request was made that the patient be examined and the status of the right kidney reported.

The lower pole of the right kidney could be felt on deep inspiration. The left could not be palpated. On account of the patient's condition and the fever, intravenous rather than retrograde visualization of the upper portion of the tract was suggested.

An intravenous urogram revealed good function on either side. There was no encroachment on the pelvis or the calices, but there was an enlargement of the right kidney, with a bulging on the lateral side suggesting a renal tumor.

I suggested further roentgen studies of the chest for metastases. This examination was made on September 29.

The report was: "Stereoscopic examination of the chest does not show any findings typical of metastatic process."

The question was raised whether the febrile state might be due to degeneration in the uterine fibroids, and Dr. R. J. Frodey, gynecologist in chief, was asked for an opinion.

Dr. Frodey reported: "The pelvic organs may be excluded as a possible source of the pyrexia for the following reasons:

1. No tenderness is revealed on palpation of the lower part of the abdomen and bimanual palpation of the pelvic organs.

2. There is no evidence of pelvic exudate in the adnexa or surrounding tissues.

3. Dilatation and curettement exclude possible pyometria or septic endometritis.

4. Some type of degeneration of a fibroid was not likely present as the tumors were all small and not tender, and none were pedunculated."

A diagnosis of right renal tumor and uterine fibromyomas was made, and after a further transfusion of 500 cc. of citrated blood the patient was operated on (October 17).

Operation.—Nitrogen monoxide and ether anesthesia was used. The cervix was dilated, and the uterus was curetted. The scrapings were meager and not suggestive of malignant disease. Fifty milligrams of radium (4 to 12.5 mg. needles in a silver capsule covered with rubber) was placed in the uterine cavity to remain for forty-eight hours.

Fig. 3.—Kidney and tumor.

The patient was placed in position for a right nephrectomy. The kidney was exposed through a right lumbar incision; complete dislocation of the kidney revealed a mass at the lower anterior border. A clinical diagnosis of hypernephroid tumor was made, and the right kidney was removed. There was no visible or palpable evidence of extension of the tumor beyond the capsule. The vascular pedicle seemed to be free from extension of the neoplasia.

Pathologic Report.—The right kidney measured 13 by 9.5 by 8 cm. A mass measuring 9 by 6 by 4 cm. projected from the center of the anterior surface of the kidney. The tumor was made up of many small nodules, all of which were

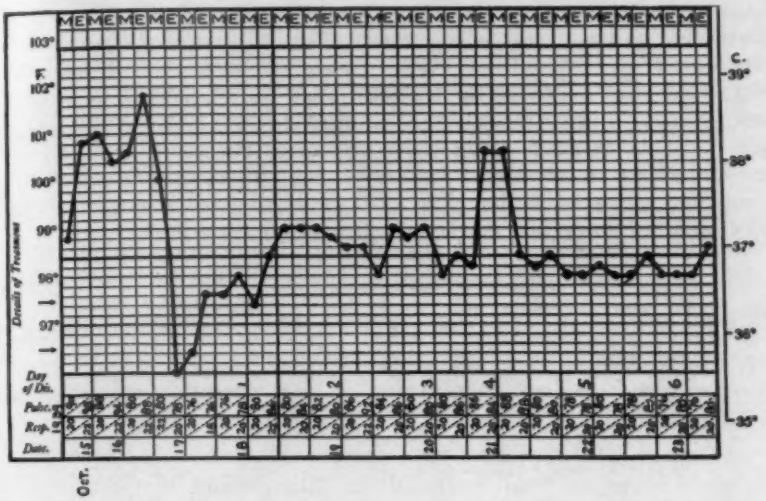

Fig. 4.—Record of the patient from October 15 to 23. On October 16 a transfusion of 500 cc. of citrated blood was given. On October 17 right nephrectomy was performed. On October 18, the radium which had been placed in the uterine cavity at the time of operation was removed. On October 22 the packing was removed.

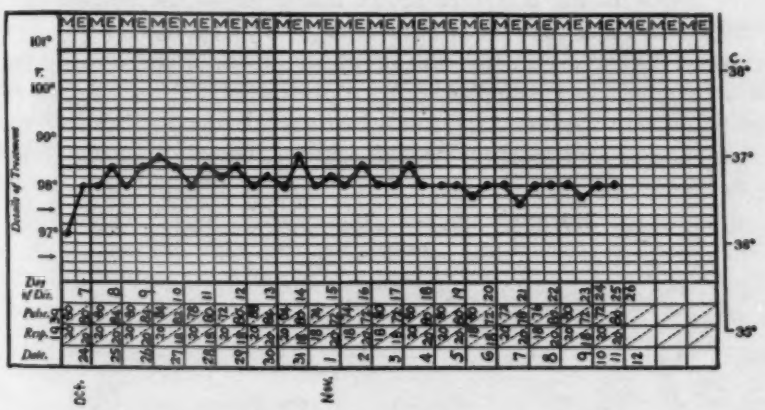

Fig. 5.—Record of the patient from October 24 to November 12. On October 25 the clips were removed.

entirely encapsulated. On section of the tumor the surface of the neoplastic mass was convex, yellowish red and very soft, with a necrotic center. The tumor compressed the pelvis of the kidney but did not invade this structure. On micro-

scopic study the essential cell was a large, clear cell, polyhedral to columnar, with a large spindle-shaped polyvesicular nucleus. Both types of mitotic cells were present. The arrangement of the growth was in wide sheets and strands of anastomosing cells. The stroma between the tumor cells was scant, vascular and delicate. A microscopic diagnosis of hypernephroid tumor of the kidney was made. There were no tumor cells in the several pieces of perirenal fat that were submitted for examination. There was no evidence of tumor in the renal vein.

Postoperative Course.—The immediate fall in temperature following the nephrectomy and the prompt return to normal were dramatic. On only one occasion in the first four postoperative days did it rise above 99 F. From then on it remained at the normal level until the patient was discharged, on the twenty-fifth postoperative day. The nausea, vomiting and uterine bleeding subsided, and the patient left the hospital free of all symptoms.

COMMENT

I think this case of extreme interest by reason of the obscure and unexplained febrile state. Repeated careful investigations as to the usual cause of fever were not enlightening. There was nothing in the history or in the symptoms to suggest the kidney as the source, as the usual symptoms of renal neoplasm were completely absent. It was only when the plain roentgenogram revealed the enlargement that attention was directed to that organ, and urologic investigation indicated the presence of the growth. Its removal was followed by complete subsidence of the fever, nausea and vomiting.

SUMMARY AND CONCLUSIONS

A review of the literature shows that fever as the initial and only symptom in renal tumor has been infrequently reported.

Renal tumor should be considered in the differential diagnosis of the condition of any patient who has a protracted and unexplained fever associated with weakness and loss of weight.

Another case of renal tumor with fever as the only symptom is added to the literature.

GAS GANGRENE

WITH SPECIAL REFERENCE TO THE IMPORTANCE OF WOOL AS A SOURCE OF CONTAMINATION

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Every great war has always been more destructive than constructive from the medical point of view. However, certain facts have come out of the results of destruction which, when properly evaluated, have done something for the advancement of knowledge. The studies of shock, hemorrhage, compound fractures, thoracic surgery and the care of wounds during the World War have all brought about improvement in surgical treatment. The care of wounds, particularly with regard to infections, is certainly better understood since surgeons have had time to evaluate the accomplishments of surgery since 1918. In the present state of world unrest, surgeons may again be faced with the necessity for studying wounds, particularly with regard to the anaerobic infections.

The history of gas gangrene has been reviewed frequently, and another such account would be superfluous. The incidence of this infection in civil life, the source of contamination and the methods of prevention are more worthy of immediate consideration.

In civil life the incidence of gas bacillus infection is still sufficiently high to warrant some further study of this formidable disease and, in view of the gravity of the infection, further efforts to reduce its morbidity and mortality. The frequency of gas bacillus infection has been reviewed in many recent publications. Callander, Haim and Maximov [1] reported 109 cases, with a mortality rate of 51 per cent; strangely, the death rate from infections of the lower extremity was over 60 per cent and that from infections of the upper extremity only 10 per cent. Ghormley [2] reported 33 cases observed in a five year period at the Mayo Clinic and cited the figures of Millar, who reported a death rate of 48.52 per cent

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1. Callander, C. L.; Haim, A., and Maximov, A.: Gas Gangrene: An Analysis of One Hundred and Nine Cases Encountered in Civil Practice, Am. J. Surg. **42**:811-823 (Dec.) 1938.

2. Ghormley, R. K.: Gas Gangrene and Gas Infections, J. Bone & Joint Surg. **17**:907-915 (Oct.) 1935.

during the World War. Coller,[3] in a comprehensive review, cited certain French observers as stating that the disease proves fatal in about three fourths of the cases. This was prior to the work of Kelly with roentgen treatment and also to the use of sulfanilamide. Eliason and his associates[4] concluded that the death rate is proportionate to the promptness with which treatment is instituted. The recent report of Mitchell and his associates,[5] who sent a questionnaire to all general hospitals of fifty or more beds in the state of New York, yielded 135 proved cases and 73 more in which the information was incomplete. They concluded from this report that infections with spore bearers that produce gas are as frequent as tetanus.

It is not my intention to go into a detailed study of the pathologic and bacteriologic aspects of this type of infection, as more interest attaches to the clinical aspects. No study of gas gangrene would be complete, however, without some reference to the bacteriologic picture, to the type of wound which favors development of this infection and, in my opinion, to the seasonal incidence of the disease. Laboratory studies have been ably done by trained workers, who have devoted much time and study to these phases of the subject (Pasternack;[6a] Pasternack and Bengston[6b]).

Since the epoch-making studies of Weinberg and Sequin[7] in 1918, one cannot fail to be impressed with the great variety of organisms associated with gas gangrene. From these studies it would appear that the same organisms can produce different phenomena under different cultural conditions. Not only is this true, but the same organism may appear in the literature under different names. According to Pasternack,[6a] "Even such a well-known species as B. welchii appears in the

3. Coller, F. A., and Perham, W. S.: Gas Gangrene in Civil Surgery, Mil. Surgeon **81**:27-38 (July) 1937.

4. Eliason, E. L.; Erb, W. H., and Gilbert, P. D.: Clostridium Welchii and Associated Organisms: Review and Report of Forty-Three Cases, Surg., Gynec. & Obst. **64**:1005-1014 (June) 1937.

5. Mitchell, O. W. H.; Bryant, T. L., and Chapman, O. D.: Morbidity and Mortality in New York State (Exclusive of New York City) Based on General Hospital Reports for Years 1932-1936 Inclusive, New York State J. Med. **38**: 1022-1025 (July 15) 1938.

6. (*a*) Pasternack, J. G.: The Cardiorenal Toxic Properties of the Toxin of Vibrion Septique in Animals, Am. J. Path. **14**:683-684 (July) 1938. (*b*) Pasternack, J. G., and Bengston, I. A.: The Experimental Pathological Changes Produced by the Toxin of Clostridium Histolyticum in Animals, Pub. Health Rep. **55**:775-784 (May 3) 1940; The Experimental Pathology and Pathologic Histology Produced by the Toxin of Vibrion Septique in Animals, Bulletin 168, United States Treasury Department, Public Health Service, National Institute of Health, 1936.

7. Weinberg, M., and Sequin, P.: La gangrenè gazeuse, Paris, Masson & Cie, 1918.

literature under four names." Most observers, however, seem to recognize a few main groups, and identification of the many subvarieties is dependent on different cultural characteristics. Clostridium welchii, which is the organism most frequently identified, is placed in the group that requires sugar for its propagation; hence, wounds of muscle and the presence of "muscle sugar" would seem to be favorable factors. Some of the other gas producers seem to be proteolytic in their action.

Most infections caused by the gas-producing organisms are mixed infections. Eliason and his co-workers [4] referred to infections with Cl. welchii and associated organisms. The incidence of the various species of clostridia as found in war wounds was best summarized by Gay and his co-workers: [8] in 308 war wounds, Cl. welchii was present in 85 per cent; Clostridium sporogenes, in 35.4 per cent; Clostridium oedematis maligni, in 17.2 per cent; Clostridium novyi, in 12.6 per cent, and Clostridium fallax, in 6.4 per cent. Since these infections are usually mixed, it is clear that a polyvalent serum would be desirable for prophylaxis and treatment, and such a serum would be difficult to prepare. Of course, the predominance of the organism of Welch enables one to concentrate attention on this anaerobe.

SOURCE OF CONTAMINATION

The matter that has chiefly interested my associates and me in connection with this problem is the source of contamination. Most students of the subject agree that soil contamination is an essential factor and that the more highly "manured" the soil the greater is the likelihood of infection. This belief is supported by the accepted fact that the organisms are normal inhabitants of the gastrointestinal tracts of domestic animals. In this connection I wish to note that in reporting the incidence of various diseases in the Italo-Ethiopian War, Castellani, in his verbal report to the Orleans Parish Medical Society on March 22, 1937, said that there were no cases of gas gangrene. In the same connection, the report of Ranson [9] from Shanghai, China, is also striking. While his contribution had to to do with gunshot wounds of the chest, he said:

> . . . Although every wound was an infected one, the virulence of the organisms appears to have been less than that of those met with in France and Flanders. One reads of the high proportion of cases of gas gangrene and tetanus met with during the Great War; here such cases were comparatively rare.
>
> Differences in the bacterial content of the soil doubtlessly account for this. The Chinese make use of human excreta for fertilizing purposes, and, although

8. Gay, F. P., and others: Agents of Disease and Host Resistance, Springfield, Ill., Charles C. Thomas, Publisher, 1935.

9. Ranson, F. T.: Notes on Gunshot Wounds of the Chest, J. Thoracic Surg. **9**:278-290 (Feb.) 1940.

this practice fosters the spread of intestinal diseases, soil treated by human excreta is freer from the germ of tetanus and the organisms causing gas gangrene than is soil treated with horse excreta.

While all domestic animals harbor the anaerobic organisms, including both the gas producers and the tetanus bacillus, the sheep is a more important source of infection in human beings than are the others, because of the fact that its wool is used for clothing. My associates and I have observed that contamination with woolen clothing is a common source of infection. In 1926, at my suggestion, Gage [10] studied some samples of clean wool and was able to grow spore-bearing organisms in practically all instances. Given a favorable type of wound (muscle injury) and contamination with wool clothing, one has the ideal conditions for development of gas bacillus infection, almost as positively as the small boy who has a punctured wound from stepping on the garden rake presents the ideal conditions for development of tetanus. In this climate the populace dresses in cotton clothing during the hot months, and I have endeavored to show that the incidence of gas bacillus infection is less frequent in the seasons when wool garments are not worn. It must always be kept in mind, however, that contamination with dirt is just as dangerous.

With the assistance of my resident, Dr. D. B. Williams, I have collected the cases from the Charity Hospital in New Orleans during a ten year period, from 1930 to 1939 (table 1) and have analyzed them according to seasonal incidence (table 2) and according to mortality in relation to type of injury (table 3), location of injury (table 4) and type of treatment (table 5).

Our figures show a total of 73 cases of gas gangrene during the ten year period, with 28 deaths, or a mortality of 38.4 per cent. During this same period the number of cases of tetanus was 341.

We have studied the seasonal incidence of the disease because we believe that the wool clothing usually worn in the cooler months is an important source of contamination, but the hospital records usually make no mention of the type of clothing worn by the patient, and we cannot arrive at any definite conclusion. We can assume, however, in view of our experimental findings, that there should be a definite increase in the number of cases in the cooler months, when wool clothing is more likely to be worn, and this is partially borne out by the seasonal incidence shown in table 2.

Following up the studies of Gage at my request, Dr. J. R. Schenken,[11] of the department of bacteriology of the Louisiana State University

10. Gage, I. M.: Gas Bacillus Infection: A Frequently Unnoticed Source in Civil Life, with Report of Four Cases, Am. J. Surg. **14**:177-184 (Oct.) 1926.

11. Schenken, J. R.: Personal communication to the author.

TABLE 1.—*Incidence of Gas Gangrene According to Years (Charity Hospital of Louisiana at New Orleans)*

Year	Number of Cases	Deaths	Mortality, Per Cent
1930	10	5	50.0
1931	10	2	20.0
1932	9	4	44.4
1933	8	3	37.5
1934	10	2	20.0
1935	8	4	50.0
1936	5	1	20.0
1937	9	4	44.4
1938	1	1	100.0
1939	3	2	66.6

TABLE 2.—*Seasonal Incidence of Gas Gangrene*

	Number of Cases
December, January, February	16
March, April, May	15
June, July, August	15
September, October, November	27

TABLE 3.—*Conditions Complicated by Gas Gangrene (1930 to 1939)*

Condition	Hospital Admissions	Complicated by Gas Gangrene	Due to Gas Gangrene: Deaths	Due to Gas Gangrene: Per Cent
Compound fractures	813	23	8	34.8
Gunshot wounds	2,333	23	9	39.1
Crushing injuries	408	13	3	50.0
Gangrene (diabetic and arteriosclerotic)	548	6	3	50.0
Lacerations; stab wounds	3,489	4	2	50.0
Other conditions	.....	4	3	75.0
Total incidence of gas gangrene		73	28	38.4

TABLE 4.—*Mortality from Lesions of the Extremities in Cases of Gas Gangrene*

	Number of Cases	Deaths	Mortality, per Cent
Lower extremity	53	22	41.5
Upper extremity	15	3	20.0

TABLE 5.—*Mortality in Relation to Treatment of Gas Gangrene*

Treatment Used	Number of Cases	Deaths	Mortality, per Cent
Amputation, no serum	11	3	27.3
Amputation plus serum	25	7	28.0
Incisions, débridement, serum	14	4	28.6
Serum alone	2	2	100.0
Operation, serum, roentgen therapy	4	1	25.0
Serum, roentgen therapy, no operation	3	3	100.0
Operation, roentgen therapy, serum and sulfanilamide	2	1	50.0
No specific treatment	6	5	83.0

School of Medicine, has made cultures of some samples of new wool and has submitted the following report to me.

Material and Methods.—Twelve pieces of woolen cloth were obtained from a manufacturer's sample catalog and were cut in half. One half of each piece was dry cleaned and steam pressed; the other half of the same piece was untreated.

Two samples, each measuring 2.5 by 1 cm., were cut by a cautery from each half piece (48 samples in all). Each sample was inoculated into a separate tube of brain broth, which was then heated in a water bath at 80 C. for forty-five minutes. The surface of the medium was covered with a 2 cm. layer of sterile melted petrolatum, after which the cultures were incubated at 37 C. for fourteen days.

Smears of the broth, stained by Gram's method, were examined microscopically as soon as gas formation was first noted. All positive cultures were later additionally examined to observe spore formation. Two smears of the cultures in which no gas had formed were examined, the first after seven days of incubation and the second after fourteen days.

Samples of cotton, rayon, linen and silk material (12 in all), none of which contained any wool, were obtained from a manufacturer's catalogue and were treated exactly as the woolen samples had been, with cultures made in the same manner.

Results.—Gram-positive spore-bearing anaerobic gas-forming bacilli, morphologically compatible with the members of the Clostridium group, were cultured from one or more of the small samples secured from 11 of the original woolen samples. Cultures of the twelfth sample were sterile. Dry cleaning and steam pressing did not materially alter the incidence of the organism. Gas bacilli were not, however, found in any of the 12 samples of the material which did not contain wool.

This confirms the fact that contamination with clean wool in certain types of wounds should be considered a precursor of gas gangrene. We have observed 2 instances in which gas bacillus infection followed hypodermic injections, 1 instance in which ordinary senile dry gangrene was transformed into gas gangrene and 1 burn that became infected. Interestingly enough, in each of these instances wool blankets had been in contact with the skin or with a raw surface.

The sheep, which has been accused as the domestic animal most likely to be the permanent host of the organisms, is not common in this vicinity, so if one accepts the speculation that wool is the most likely source of contamination one must also note, as is evident from the report of Dr. Schenken, that spore-bearing organisms are present on wool after it has passed through all the processes incident to its final use as a finished garment.

TREATMENT

Treatment should be divided into two phases: (1) prophylaxis and (2) treatment of established infection.

The best treatment of this disease is prevention of the anaerobic infections, and certain definite rules can be formulated with this end

in view. Once infection with the group of anaerobes capable of producing gas gangrene has developed far enough to be recognizable, a certain mortality is inevitable. However, the therapeutic armamentarium has improved so much in the last few years that physicians do not fear this disease as much as in the past. Certainly, the prophylactic and therapeutic use of serum has done some good, and when one adds treatment with roentgen rays and with sulfanilamide the necessity for radical operation is materially diminished. Some observers go so far as to discount entirely the necessity for amputation and even doubt the advisability of free incision and of treatment with local agents other than the roentgen rays. In reviewing the vast literature of the past few years, one can find enthusiastic advocates of many types of treatment and even statistics to show their value. But judgment must be reserved, for, to quote the editors of the 1939 "Year Book of General Surgery," "Only one hundred years ago the disciples of Benjamin Rush were claiming that practically all diseases should be treated by blood letting." [12] In spite of all methods introduced for treatment of this disease, the mortality is still high, and one cannot evade the fact that prophylaxis for certain types of wounds and early clinical recognition confirmed by bacteriologic examination are the most dependable means of reducing the mortality rate of this disease.

In view of the foregoing statements, it would be wise to consider wounds of the extremities, especially those involving muscle and those contaminated with wool or dirt, as potentially infected with gas gangrene. Wounds of the calf of the leg associated with laceration and devitalization of tissue are especially liable to show subsequent development of organisms capable of producing gas gangrene. Under these circumstances the obvious emergency treatment of such wounds is thorough débridement, with the wound left open, and administration of the antitoxin which is now available, the possibility of secondary closure being kept in mind.

Some recent suggestions by Keating and Davis [13] seem particularly pertinent. These authors suggested the prophylactic use of the roentgen rays for "dirty wounds" as being effective against the gas-forming and other organisms, thereby decreasing the necessity for mutilating surgical procedures.

Should evidence of spreading infection with severe constitutional symptoms develop, the principle indicated by the aphorism of Eliason that the mortality is dependent on the promptness with which treatment is instituted must be rigidly obeyed. While cultures should always be

12. Graham, E.: Year Book of General Surgery, Chicago, The Year Book Publishers, Inc., 1939, p. 95.

13. Keating, P. M., and Davis, F. M.: Prophylactic Treatment of Wounds in War, Mil. Surgeon **86**:235-240 (March) 1940.

made for confirmation, the delay incident to waiting for such bacteriologic studies may be a determining factor in the patient's life. Usually it takes twenty-four hours to get a report of wound culture, and gas bacillus infections spread so rapidly that twenty-four hours is too long to wait for confirmation of the diagnosis.

The early diagnosis of gas gangrene in civil life dates practically from 1918. Prior to this period the simultaneous appearance of a severe infection and of "gas" in the tissues was the only known sign. As these are antemortem phenomena, the patients were rarely saved by treatment. Amputation of the involved extremities was the only treatment and was always frankly an operation of despair.

Usually the inception of a gas bacillus infection makes itself known by certain local and constitutional changes which should require inauguration of the "curative" measures which are at the physician's disposal. Local swelling and a dry wound with a peculiar odor which has been variously described as a "mousy" or a "rotten meat" smell are significant. The khaki-colored skin in the white race is easily recognized. The patient goes into a state which resembles surgical shock, and even when recovery occurs there is a long period during which the myocardium shows evidence of damage.

Since the work of Kelly and his associates [14] on roentgen treatment, the older procedures have been abandoned by many as unnecessary. The local use of oxidizing agents in the presence of anaerobic infection has been given serious thought. Such agents as potassium permanganate, specific quinine solutions, hydrogen peroxide and pure oxygen have all had their day. Getting these drugs into contact with the organisms without tissue destruction is a "consummation devoutly to be wished," but, considering the method of spread, this cannot be achieved.

In the light of recent experience, the treatment of established gas bacillus infection should be considered under several headings. The curative value of the serum is debatable, but it should always be used. When the work of Kelly and others is considered, one must accept the fact that roentgen treatment lowers the mortality. The report [14b] of a death rate of 11.3 per cent by Kelly and his co-workers certainly represents a decided improvement and gives strong support to the contention that amputations and extensive incisions should be abandoned. According to the observations of Faust,[15] who gives the technic in detail,

14. (*a*) Kelly, J. F., and Dowell, D. A.: Present Status of the X-Rays as an Aid in the Treatment of Gas Gangrene, J. A. M. A. **107**:1114-1118 (Oct. 3) 1936. (*b*) Kelly, J. F.; Dowell, D. A.; Russum, B. C., and Colien, F. E.: Practical and Experimental Aspects of Roentgen Treatment of Bacillus Welchii and Other Gas-Forming Infections, Radiology **31**:608-619 (Nov.) 1938.

15. Faust, J. J.: Report on X-Ray Treatment in Gas Gangrene Cases, Radiology **22**:105-106 (Jan.) 1934.

roentgen therapy causes hydrogen peroxide to be generated in the tissues, and this is the important factor in combating the growth of the organisms and in minimizing generation of the toxin.

The use of sulfanilamide has not been neglected, and, while this drug does not seem to control the specific infection, it may be of value in controlling the growth of the ordinary pyogens, thereby destroying symbiosis. Since the ordinary pyogens use the oxygen present in the tissues and permit the anaerobes to flourish, this effect of sulfanilamide should be of value.

This discussion brings one finally to the value of free incision and amputation. I have always felt that, since spread of the infection is longitudinal, along the muscles, amputation may be advisable to prevent this spread. It is a common observation that in cases in which the calf is involved there is a tendency for the progress of infection to hesitate temporarily at the knee. This interval presents an excellent opportunity for amputation to prevent spread beyond. On account of the arrangement of the musculature about the shoulder, the phenomenon is not observed in this location. I have never resorted to amputation when the arm was involved. Again, even when the infection has been controlled there may be large areas of sloughing, and the patient's recovery may be accelerated by choosing amputation rather than waiting for spontaneous separation of the dead areas to take place. This is especially true of wounds of the leg.

Pasternack has called attention to the susceptibility of the heart muscle to the toxin of vibrion septique, and, as has been noted, the condition of this organ must be watched for a long time even after the patient has recovered from his infection.

SUMMARY

Gas gangrene is sufficiently important in civil life for surgeons to give it serious consideration. In conformity with the bacteriologic report of Dr. Schenken, contamination with any woolen article, even clean clothing, makes rigid prophylactic measures imperative. It is urged that physicians suspect anaerobic infection with production of gas gangrene whenever wounds of the extremities involving muscle have been contaminated with wool or with soil. Such wounds should be treated by wide incision (then being left open) or by thorough débridement.

Prophylactic administration of the specific serum seems to be of definite value, and it seems possible from the report of Keating and Davis that the prophylactic use of roentgen therapy is justified.

In the care of a wound in which the factors that favor gas bacillus infection are present, eternal vigilance must be exercised; in the face of suggestive signs of such infection, specific treatment should be started at once. Cultures for confirmation should always be made, but the delay

incident to waiting for a report represents valuable time lost. The relative values of the known beneficial factors may be debatable, but since there is some benefit from the anti-gas-bacillus serum and from sulfanilamide and since there is positive evidence of benefit from the use of the roentgen rays, all three should be used. Wide incision and amputation still have their places and must be used when conditions warrant, though the necessity for the use of such measures has materially diminished.

As with all diseases, rules are dangerous, and one must individualize the treatment, making full use of all known beneficial agents.

GANGRENE OF THE SIGMOID FLEXURE OF THE COLON DUE TO VOLVULUS

RECOVERY OF A CHILD; SPONTANEOUS ANASTOMOSIS BETWEEN THE DESCENDING COLON AND THE RECTUM

EDWIN M. MILLER, M.D.
CHICAGO

Acute intestinal obstruction produced by volvulus of the sigmoid flexure of the colon with complete gangrene is very rare in a child, but that such a patient should not only recover but have a spontaneously developed anastomosis between the descending colon and the upper part of the rectum is unique and, therefore, seems worthy of publication.

Volvulus, or twisting of the intestines, may occur in any portion of the gastrointestinal tract but is most commonly met with in the sigmoid flexure, the cecum and the ascending colon. It is predisposed to by an abnormally long mesentery combined with a narrow base between the afferent and the efferent loops. The presence of adhesions and tumors in the mesentery or in the bowel itself is often a contributing factor. Constipation unquestionably plays an important role. It occurs more often in males than in females, usually affects persons beyond middle life and accounts for perhaps 15 per cent of all forms of intestinal obstruction. Children are rarely affected by volvulus, although twisting of the entire small bowel on the axis of the superior mesenteric artery in combination with an incomplete rotation of the cecum in infancy or early childhood may lead to partial or even complete obstruction of the duodenum at its junction with the jejunum.

The experience described here has given my associates and me one of the greatest thrills we have encountered in surgical practice.

REPORT OF A CASE

A 12 year old Negress was admitted to the children's surgical ward of the Cook County Hospital at 10:50 p. m. on Friday, Oct. 13, 1939, with the diagnosis of ruptured appendix with peritonitis. The temperature was 101 F.; the pulse rate was 144, and the respiratory rate was 26. The onset had been acute, the patient having been awakened from sleep at 5 a. m. on October 12 with severe abdominal pain. This was followed during the day by nausea and persistent vomiting. Magnesium citrate given by mouth and repeated enemas had failed to give her relief. On admission to the hospital she looked extremely ill, was markedly dehydrated and was begging for something to make her sleep. Her abdomen

From the Surgical Department of the Cook County Hospital.

was greatly distended. A Levine duodenal tube was immediately introduced, intravenous fluids were started and enough morphine was given to make her comfortable. The following morning a roentgenogram of the abdomen (fig. 1) showed one greatly distended loop of large bowel. The abdomen was silent and tympanitic throughout, and a marked bulging was noticed, mostly in the left upper quadrant. At 2 p. m. she was brought to the operating room, and the abdomen was widely opened through a long right rectus incision. A considerable amount of foul-smelling, blood-stained fluid escaped. The entire sigmoid flexure of the colon had been twisted and had become gangrenous. It was so greatly

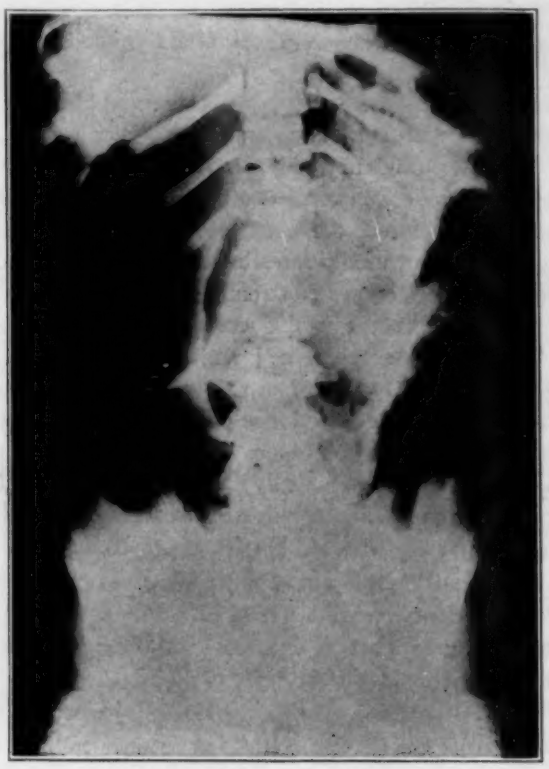

Fig. 1.—M. M., aged 12 years. There was acute intestinal obstruction due to volvulus of the sigmoid flexure of the colon, with gangrene. The roentgenogram shows the enormously distended sigmoid flexure occupying almost the entire right half of the abdomen.

distended that we were able only with difficulty to deliver it from the abdomen without fear of perforation. Moreover, this gangrenous loop extended so far into the depth of the left flank that resection would have been impossible even if the patient's condition had permitted it. A very conservative plan was therefore adopted. Several strips of petrolatum gauze were gently packed closely about it; the wound was quickly brought together; the huge bowel was slowly deflated of its foul gas and liquid fecal contents by means of a large syringe; copious dry dressings were applied, and the child was returned to the ward, every one fully expecting her to die before many hours had passed.

Fig. 2.—*A*, postoperative color photograph showing the exteriorized gangrenous sigmoid flexure of the colon. *B*, remnant of the sloughing sigmoid flexure at the lower end of the gaping wound. *C*, patient just before leaving the hospital. The continuity of the colon is completely reestablished.

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On the following morning, however, the child's condition was surprisingly good, and on Monday (October 16) the exteriorized, greatly distended black bowel (fig. 2 *A*) was again deflated by a free incision along the dependent border. On October 17 her condition was excellent; her temperature was lower, and she was asking for food. The Levine tube was removed, and a considerable portion of gangrenous bowel was trimmed off. Steady progress was made from that time on, a little more sloughing tissue coming away each day until by October 24, ten days after the operation, only a small amount of black slough could be seen in the depth of the granulating wound (fig. 2 *B*).

Fig. 3.—Roentgenogram taken after complete sloughing of the sigmoid flexure of the colon, showing the spontaneous channel between the proximal and distal segments of bowel.

The interesting and strange aspect of her progress was first observed on November 11, almost one month after operation, when she passed a normal stool by rectum. Much to our amazement this continued to take place without interruption each day thereafter, the excreta gradually increasing in amount until perhaps one half of the fecal content of the colon was passing through the normal way, thus effectively establishing spontaneously a narrow channel around the opening in the abdominal wound. Before long, however, we began to consider seriously the advisability of more completely reestablishing the continuity of the bowel by operation, and, therefore, barium sulfate was introduced both from above and from below. A roentgenogram (fig. 3) made on November 21 gave

us an excellent graphic demonstration not only of the length of the remaining descending colon but of its proximity to the upper part of the rectum, suggesting the feasibility of making a wide anastomosis which would effectively short circuit the area occupied by the colostomy opening in the lower portion of the rapidly healing wound from the right rectus incision. This operation was carried out on Jan. 29, 1940, through a clean field on the left side, a lateral anastomosis being easily accomplished without tension on the line of sutures. From then on her progress was very rapid. The wound healed without infection, and as the days went by more and more stools were passed the normal way, and conse-

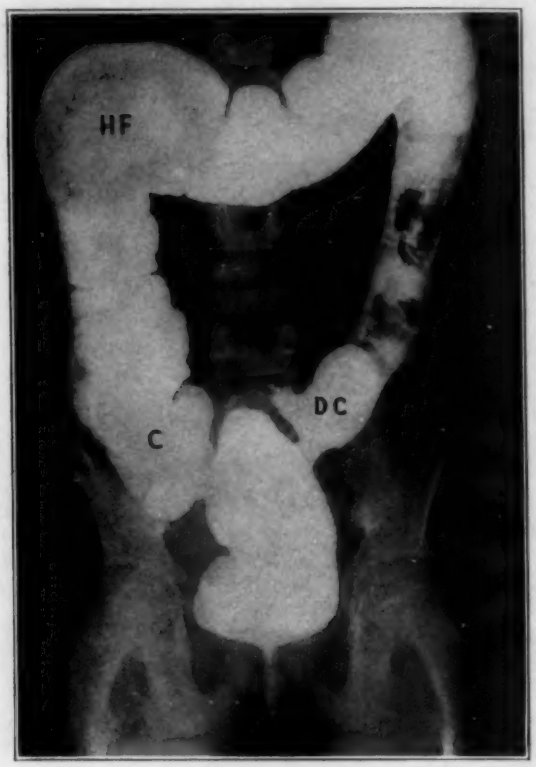

Fig. 4.—Roentgenogram taken after a barium sulfate enema, showing the continuity of the left side of the colon after the final operation. *HF*, hepatic flexure; *DC*, descending colon; *C*, cecum.

quently less and less fecal material came through the original wound. It therefore became a simple matter to carry out surgically the third and final procedure (February 16), not only completely excising the extensive scar which had resulted from slow healing of the granulating wound and separating the many loops of ileum which had become firmly matted together in this area but securing firm closure of the original incision. The success with which this was accomplished may be realized by a glance at a roentgenogram (fig. 4) made on March 2, after a barium sulfate enema, and at a "kodachrome" picture (fig. 2*C*)

of the child taken on March 1, just six days before she was discharged to her home, a healthy-looking, happy girl with a normally functioning gastrointestinal tract.

CONCLUSION

I would emphasize the advisability of being very conservative at the initial operative procedure in the presence of such extensive gangrene and would point out the feasibility of complete reestablishment of the continuity of the left side of the colon.

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SURGICAL MANAGEMENT OF SACROCOCCYGEAL AND VERTEBRAL CHORDOMA

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AND
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Chordoma is so rarely encountered that individual experience is limited, and no clearcut plan of surgical attack on the tumor as it may develop in the different levels of the cerebrospinal axis has been established. A survey of cases reported in the literature reveals a variety of methods of treatment employed, but the results have been far from satisfactory. Sacrococcygeal and vertebral lesions only will be considered in this paper. A procedure will be presented that may permit a more thorough extirpation of lesions in the sacral region; the value of spinal fusion as an adjunct to laminectomy in dealing with vertebral tumors will be discussed, and 3 illustrative cases, heretofore unreported, will be added to the literature.

Chordoma is a tumor arising from the remnant of the notochord. It may occur anywhere in the cerebrospinal axis, from the sphenoid bone to the coccyx. In the order of frequency it is found in the sacrum, the base of the skull and the lumbar portion of the spine, but it may occur in any of the vertebrae. If vertebral in origin, the tumor usually arises in the vertebral body.

Chordomas are difficult to eradicate on account of the usual antevertebral position, the bony origin, the intimate relation to the spinal nerves and, at times, the actual invasion of the dura and spinal cord. Thus block excision is applicable only to the lesions in the sacrococcygeal region, which fortunately are the most numerous. Such tumors should lend themselves to block removal unless they have progressed too extensively, for they usually show a tendency to remain encapsulated, recur locally and metastasize late in the disease. They are of more common occurrence in the lower part of the sacrum or in the coccyx than in the upper segments of the sacrum. Very rarely does invasion of the rectum or of the bladder take place.

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In a compilation of cases of chordoma from the literature [1] Mabrey in 1935 found a total of 150 reported for all levels. Of these, the tumors in 87 were sacrococcygeal. Other cases prior to that date but unreported by him and 32 more to the present time, inclusive of 1 reported in this article, raise the number to 122, in 62 of which the tumors were antesacral, in 41 retrosacral and in 19 central. Sufficient data for adequate evaluation were available in but 87 of the total number.

By far the great majority of chordomas become manifest between the ages of 40 and 70 years. Men are afflicted twice as often as women. A history of trauma with injury to the lower part of the back or to the gluteal region is obtained in one third of the cases.

Pain is by far the most common and salient symptom and is present in over half the cases. Tumor in the sacral, the gluteal or, less often, the perineal region is frequent. Rectal symptoms, either severe constipation or incontinence, occur in 20 per cent of the patients. Occasionally obstruction supervenes, and very rarely there is bleeding by rectum. Disturbances referable to the urinary tract (incontinence and retention) are somewhat less common, as are referred nerve pains, such as sciatica.

The differential diagnosis of chordoma of the sacrum depends in great measure on roentgen examination, but even with such examination there is room for error at times. One should suspect chordoma whenever a tumor is found which causes severe pain and appears to arise from the sacrum. The tumor may be confused with sarcoma, osteoma, ependymoma of the filum terminale, carcinoma of the rectum with involvement of the sacrum, metastatic carcinoma or tumor arising from the generative organs. One should remember that chordoma seldom ulcerates through into the rectum, though this condition is sometimes reported, as is intestinal obstruction. The tumor is usually smoother, more elastic and more discrete than the malignant tumors just mentioned. Osteoma, on the other hand, is excessively hard.

The roentgen findings may be definitely suggestive. A smooth-walled area of bone destruction, usually near the midline, with a homogeneous soft tissue mass bulging out from the region of the defect, is characteristic. The diagnosis is conclusively established only by biopsy in many instances. The soft, gelatinous tumor lends itself to aspiration, and the diagnosis has been frequently proved by this means.

At operation the tumor is very vascular, and after the capsule is entered the mass is usually found to be soft and translucent. It is very

1. The ultimate result in 3 cases reported by Mabrey is known. The patients in Smith-Petersen and Hampton's case VII and Mixter and Jones case VIII each died of recurrence five years after operation. The patient in Simmon's case II died of carcinoma of the uterus nine years after operation. No pathologic confirmation of this diagnosis was obtained.

friable and is slightly yellowish after it is separated from its blood supply. The capsule is a definite structure, and there is a sharp line of demarcation between the tumor and the surrounding tissues. The characteristic picture, microscopically, is that of a more or less homogeneous mucoid intercellular substance with widely separated strands or masses of large vacuolated cells. Mitoses are rarely seen.

The three methods of treating chordoma are by irradiation alone, by operation combined with irradiation and by operation without irradiation. Although occasionally irradiation, either roentgen or radium, may be beneficial, in general the tumor is radioresistant, and little if any improvement may be expected to follow treatment. In 11 cases in which radiation alone was used, no relief was obtained in 7, and only 2 patients lived longer than twenty months, 1 dying with recurrence and metastases in six years and the other in five. Roentgen irradiation and, to a less extent, radium irradiation are valuable as palliative measures in controlling pain.

In 21 of the 87 cases an operation was done, combined with some form of radiation administered either preoperatively or postoperatively. The average duration of life is definitely increased over that observed with the use of radiation alone, but it may be safely assumed that operation was withheld and radiation alone utilized in the cases of most advanced involvement. Mabrey stated that the combined method of treatment gives the best results statistically. This is undoubtedly so, and the 2 cases in which the patients survived for the longest period after institution of treatment both fall into the group in which combined operative and radiation therapy was given. The patient in the case reported by Machulko-Horbatzewitsch and Rochlin died of angina fifteen years after the first operation, at which time coccygectomy with removal of the tumor was performed. In the intervening period three more operations, including excision of the fourth and fifth sacral segments, had been done, and a local curettage was performed some months before death. Roentgen therapy was not instituted until two months before the patient died. In Pool's case the coccyx was excised, and a 3 inch (7.6 cm.) antesacral tumor arising in the sacrum was "removed as completely as possible." The wound was packed open for radium. Nine months later there was a 3 inch recurrent mass palpable through the rectum. The mass remained stationary, and the patient was reoperated on after two years. The tumor was bony hard. No tumor cells were to be seen microscopically. Fifteen years after the first operation the patient was reported to be still alive. It is incontrovertible that irradiation could have played no part in the successful result in the former case, as roentgen therapy was instituted only two months before death. An extensive operation with removal of a large amount of

involved bone was performed in both cases and may well have been the procedure that determined the satisfactory outcome. Yet both of these cases must be included in the group in which combined operative and radiation therapy was used, and in such a small series the exceptional length of survival of 2 patients has a preponderant influence in causing the average period of survival to be the greatest observed in any group.

Operation without irradiation was employed in 55 cases. Thirteen of the patients succumbed after operation. Multiple procedures were done in a number of cases, so that the operative mortality in the 68 operations was 19 per cent. Shock was by far the most common cause of postoperative death; sepsis, pulmonary embolus, peritonitis and thrombosis of the iliac vein were also responsible for fatalities. Colostomy was employed twice, but in neither case as a preliminary stage to a block resection. In 1 instance (Lewis) it was used in conjunction with removal of the tumor through an abdominal approach, and in the other case (Albert) as the third procedure shortly before death occurred.

Reported cases of chordoma have meager follow-up notes, and in many instances the ultimate result is not given. However, there were 9 patients who received operative treatment but no radiation who lived for over three years. In 1 instance (Simmon's case) death occurred from cancer of the uterus nine years after operation on the chordoma. In another (Stewart), recurrence and metastases developed ten years after resection.

From the foregoing considerations it would appear that radical extirpation of sacrococcygeal chordomas offers the best chance of prolonged relief in spite of the high operative mortality of this procedure. We do not know whether it would be feasible to resect the upper two segments of the sacrum. Such an operation would be very difficult and even if successfully carried out would cause great disability. It is possible to resect the sacrum below this level. Such an operation should not be considered if disease of the upper part of the sacrum is too extensive. Careful roentgen examination will determine this. Other contraindications to this type of operation are involvement of the sciatic nerve and evidence of distant metastases.

To diminish the hazard of sepsis at the time of operation and in the postoperative period a preliminary colostomy has many advantages. It should be a defunctioning procedure and yet one that is readily capable of reconstruction should there be no indication for a permanent colostomy after the resection is accomplished. After the abdomen is opened and before the colostomy is done, the peritoneal cavity, the paravertebral lymph node, and liver should be examined for direct extension or metastases. A colostomy of the Devine type established in the sigmoid flexure of the colon permits preoperative cleansing of the distal segment and will relieve obstructive symptoms if present.

As soon as the colostomy is functioning well the sacrum is approached from behind. A block resection is carried out, with removal of all the structures involved, including the coccyx and the sacrum to a point definitely above the upper limit of the growth as previously determined by roentgen examination. The first and second sacral nerves will not come into the field of this procedure. One should sacrifice all the lower sacral nerves without hesitation rather than run any risk of cutting into the growth. Piecemeal removal is to be avoided, not only on account of the danger of recurrence but because of the extreme vascularity of the tumor. The vessels entering these growths are large, and careful hemostasis is important to prevent undue loss of blood. Should resection of the rectum be necessary (a procedure which has been reported in the literature [Sénèque and Grinda]) or should injury occur during operation, the preliminary divergence of the fecal stream reduces the danger of serious infection to a minimum.

With a well functioning colostomy and constant drainage of the bladder, the discomfort to the patient is reduced, the after-care simplified by elimination of use of the bed pan and the danger of wound contamination diminished. If the third sacral nerves and all below are cut there will be a considerable area of saddle anesthesia extending forward over the perineum and the external genitalia. There probably will be some loss of function of the anal sphincter, but immediate postoperative lack of function is not necessarily permanent. Vesical retention may occur, as after any pelvic procedure, and constant drainage is advantageous. Ultimately the sphincter of the bladder should be competent, though too little is known about the exact level of function of the bladder to enable one to be dogmatic on this point. It will be found that the gluteus muscles cannot voluntarily be drawn together after removal of the lower part of the sacrum. The fact that part of the origin of these muscles is left free seems to cause little if any disability.

REPORT OF CASES

CASE 1.—D. G., a married woman aged 38, was referred to us by Dr. Morris Rutenberg. There was nothing of note in her family or past history. In October 1938 she began having pain low in her back, extending out somewhat into her right buttock. This pain was increased by sitting. It was not associated with urination or defecation. There was no pain or weakness of the legs, and no numbness or paresthesia was observed. The pain was increased by motion and was incapacitating. Examination in December showed a smooth, hard, somewhat tender mass projecting into the presacral space and palpable by rectum. It was not adherent to the rectum and was about 2 cm. across. There was some tenderness of the lower part of the sacrum and coccyx and to the right of the coccyx. Roentgen examination showed a defect in the sacrum, suggestive of chordoma. An operation was performed, the mass being explored from behind and a large amount of new growth removed. A pathologic diagnosis of chordoma was made.

The pathologic report was as follows: Numerous bits of tissue, the largest about 2 cm. in diameter, were submitted. Grossly the tissue appeared to be composed of an agglomeration of cysts about 1 mm. in diameter. Microscopically, these cystlike areas were seen to represent regions largely composed of mucoid, pale blue-staining, somewhat fibrillary intercellular substance. This characteristic-appearing intercellular substance had embedded in it a variable number of tumor cells, and there was very little other stroma present. The tumor cells were large and stellate; they had indefinite walls and palely staining cytoplasm, often vacuolated. The nuclei were large, pale and somewhat irregular in size and shape; they had prominent nucleoli. Occasional multinuclear cells were observed, but few mitoses.

Roentgen treatment was instituted and continued for several months, at first with some apparent improvement. Then the pain recurred and became more severe than before the operation.

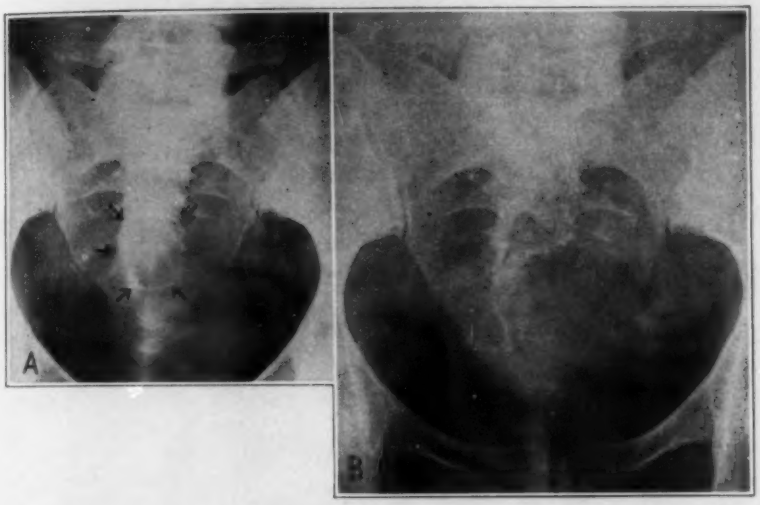

Fig. 1 (case 1).—*A*, roentgenogram taken before the first operation. *B*, roentgenogram taken two months before the second operation. Note the increase of bone destruction.

When the patient was first seen by us, on Sept. 22, 1939, it was evident that only radical measures would be of benefit. Her general condition was good, but she could do very little, on account of pain. She was taking sedatives regularly but without much relief. She complained of moderately severe constipation, but the function of the bladder was normal. The mass palpable by rectum was now about 6 cm. across. The rectum was not adherent to it but was compressed by the mass. The rectal sphincters were relaxed. There was no weakness in the legs and no change in sensation or reflexes anywhere.

The roentgenograms (fig. 1) show the progress of the disease during the time she was under observation.

On October 11 a laparotomy was performed. The mass was palpated, and it was determined that there was no involvement of the peritoneum, the retroperitoneal lymph nodes or the liver. A Devine type of colostomy was carried out. Con-

valescence from this operation was prolonged by the development of pyelitis. The abdominal wound healed perfectly, and the colostomy functioned well.

On November 29 a second operation was performed. A longitudinal incision was made over the sacrum, running nearly to the anus. The greater portion of the sacrum and the coccyx were exposed. The levator muscles and the glutei were cut away and the dissection carried up in front of the sacrum and coccyx. It was remarkable how easily the presacral tissues were separated from the sacrum

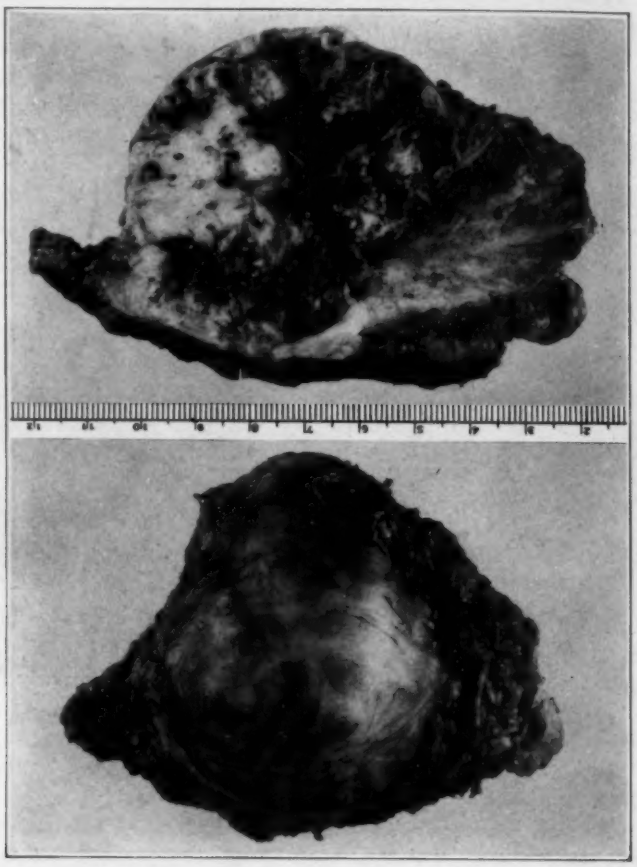

Fig. 2 (case 1).—Tumor, portion of the sacrum and coccyx removed in one block.

and the mass bulging from it. The dissection was then carried up at the sides of the sacrum, all nerves being sacrificed up to and including the third sacral on the right. It was not necessary to sever the third sacral nerve on the left. The sacrum was dissected free up to the lower edge of the sacroiliac joints. Cuts slanting toward the upper part of the sacrum were made from a little below the sacroiliac joint on each side with heavy cutting forceps, and these were connected across the midline, thus amputating the lower part of the sacrum, the coccyx and the tumor in one block. It was impossible to bring the muscles together

except in part. The superficial fascia and skin were closed, and a moderately large dead space was left, which was drained.

The pathologic report was as follows: The tumor, the coccyx and part of the sacrum had been removed intact and were surrounded by a fibrofatty capsule except over a small area. The bulk of the hemispherical tumor, measuring 8 cm. in diameter, was attached to the ventral surface of the coccyx and sacrum, projecting, however, more to the right than the left. The bones were invaded throughout their thickness, the tumor projecting about 1 cm. above the dorsal surface. On section the tumor was largely soft and gelatinous, somewhat lobulated, partly necrotic and hemorrhagic and varied from gray to yellowish to brown. Microscopically, the tumor showed less typical intercellular substance and was hence more

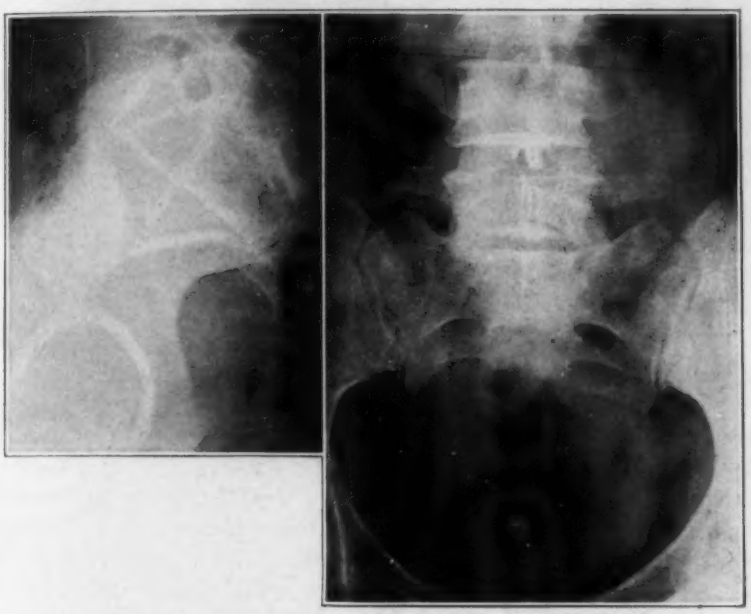

Fig. 3 (case 1).—Postoperative roentgenograms showing the extent of removal of the sacrum.

cellular. The tumor cells were otherwise similar, but a larger proportion were vacuolated.

As was expected, the wound became infected but finally healed. At first there was retention of urine and constant drainage was carried out. This was unnecessary after a week.

Her condition at the time of writing, five months after operation, is satisfactory. She has normal control of her bladder. The right side of the vulva is anesthetic, as is an area over the right side of the sacrum and the right buttock. There is no anesthesia of either leg and no change in tendon reflexes. Her gait and station are normal. There is a soft area about the scar on her back, that does not give her any discomfort. A colonmetrogram, taken by Dr. J. C. White on March 25, 1940, shows good sensation and peristalsis in the lower part of the sigmoid flexure and the rectum. The rectal sphincter is continent up to 40 cm. of water pressure. The continuity of the sigmoid flexure is now being reestablished.

As was indicated at the beginning of this paper, chordoma of the vertebral column presents a very different problem from chordoma of the lower part of the sacrum and the coccyx. It is rare indeed that a preoperative diagnosis can be made with any certainty. The outstanding features of these growths are similar to those of extradural benign tumor of the spinal canal or of some destructive lesion of the vertebral body. In common with these growths, they usually cause compression of the cord or of the cauda equina with the signs associated with such compression, namely, pain, paralysis below the level affected and block of the spinal fluid. A history of trauma is somewhat suggestive. Chordomas grow more slowly than do malignant lesions. The roentgen picture, while not as characteristic as that of sacrococcygeal chordoma, may be helpful. If the body of the vertebra is involved there may be a rounded cavity visible in it, or there may be an irregular mottled appearance similar to that seen in vertebral hemangiomas except that the mottling is coarser. There is no evidence of new bone formation as in metastatic carcinoma of the prostate; bone destruction is not as intense, nor does it show the moth-eaten appearance characteristic of most of the other forms of malignant disease of the vertebral body. In 1 of our cases (case 3) a presumptive diagnosis of chordoma should have been made by roentgen examination.

The problem of treatment also is different. In the spine one is dealing with a growth which on account of its position is not open to radical extirpation. Therefore, palliative operation and, if desired, roentgen therapy are the only measure. These tumors are of slow growth. There is a definite tendency to dislocation or to collapse of the vertebral body. When the disease is extensive we believe that after exploration and as complete removal of all tumor tissue as is possible, an early fusion operation should be performed to combat this danger. In 1 of our cases (case 2) partial dislocation took place before fusion was carried out. As a result of this experience the other patient was submitted to a fusion operation five weeks after piecemeal removal of the growth. Such an operation adds several weeks to the period of hospitalization. However, the indication for a procedure to strengthen a spine already weakened by this slowly progressive, destructive disease, plus an extensive laminectomy is clearly evident.

CASE 2.—J. W. O., a boy aged 14, was admitted to the Massachusetts General Hospital on Nov. 4, 1935. There was no history of unusual trauma to the neck. The patient had always been a strong, active boy.

One year before entrance the patient had had an attack of stiffness in his neck, with pain on motion. This lasted several days. Since that time he had had a number of similar attacks. During the last six months there had been gradual development of numbness and weakness in all four extremities. This began in his right hand and later spread to the left. It was only during the week prior to admission that the process had involved his legs. There had been no pain in

the extremities. Though weak, he could move all the muscle groups. There had been no interference with urination or defecation.

Physical examination revealed nothing remarkable except as follows: There was moderate limitation of motion in the neck, with pain on motion. There were weakness and spasticity of all muscles, including those of the shoulder girdle. Increased tendon reflexes, bilateral Babinski signs and clonus were present. There was diminution of all forms of sensation in both arms. There was no pain or numbness of the occiput.

A combined cisternal-lumbar puncture was performed, which showed evidence of block, and iodized poppyseed oil was injected into the cisterna magna. The

Fig. 4 (case 2).—Preoperative roentgenogram. Note the small area of bone destruction in the third cervical vertebra.

total protein content of the spinal fluid from the lumbar needle was 83 mg. per hundred cubic centimeters.

Roentgen examination (fig. 4) was at first thought to reveal no abnormality, but review of the plates at a later date showed a suggestion of bone destruction in the lamina and pedicle on the right side of the third cervical vertebra. Block of the iodized oil, with cap formation, was present at the second cervical vertebra.

Laminectomy on November 16 revealed a soft, reddish extradural tumor lying in front of and to the right of the cord. It seemed to arise from the pedicle and body of the third cervical vertebra and extended from the upper edge of the second to the lower edge of the third. The growth mushroomed out through the second intervertebral foramen. The pedicle and the transverse process were eroded. The

mass was removed in several large fragments, the excision apparently being complete except where it seemed to arise from the vertebral body. The right vertebral artery was surrounded by the growth. It was cut across and secured with dura clips.

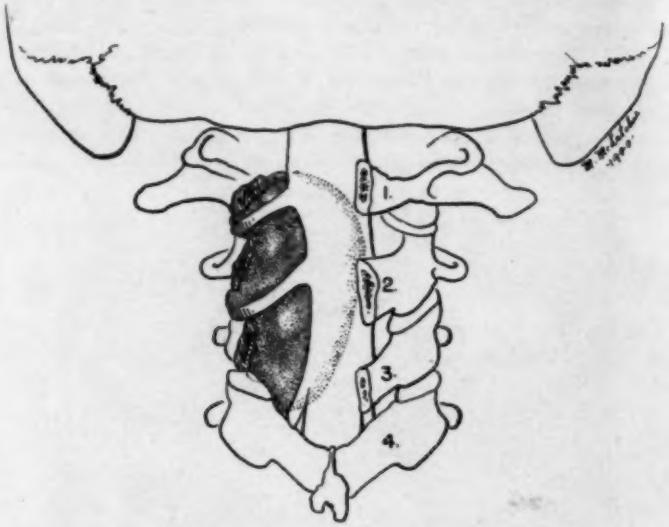

Fig. 5 (case 2).—Sketch of the tumor as seen at operation.

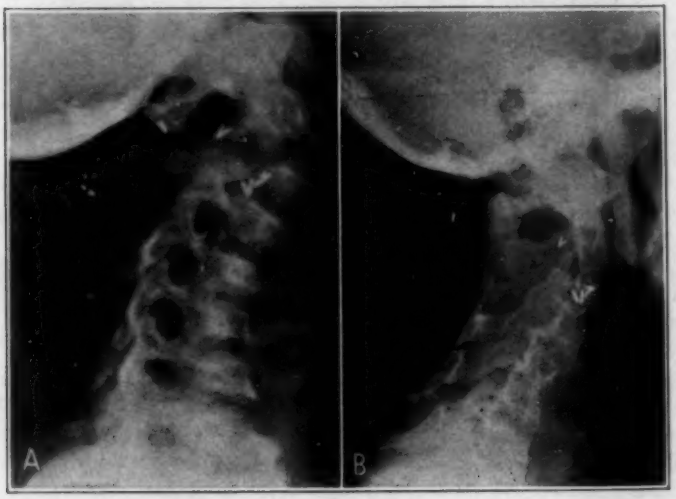

Fig. 6 (case 2).—*A*, dislocation following laminectomy. *B*, present condition. Note the reduction of the dislocation and the solid fusion.

Pathologic examination showed the tumor to be a chordoma. No mitotic figures were seen, and it was thought to be of comparatively slow growth.

All muscle weakness, sensory disturbance and reflex changes cleared up rapidly. It was realized that there was great danger of dislocation on account of the bone

destruction and the extent of the operative procedure. Notwithstanding careful immobilization, gradual dislocation took place, though without neurologic signs.

The boy was readmitted to the hospital, and a fusion operation was performed on June 16, 1936, by Dr. Edwin F. Cave.

Roentgen therapy was discussed but not advised in this case. It was thought that the tumor was of slow growth and might not recur for many years. It was felt that the massive doses necessary to influence such a growth would be unwise on account of the long life expectancy of the patient.

He has done well in every respect. When seen on Sept. 18, 1939, he showed evidence of solid fusion. There was no muscular weakness, impairment of sensation or reflex abnormality. Notwithstanding the fact that his neck is stiff, the boy is running on his school track team. This patient was quadriplegic or rapidly becoming so. The growth was extensive and, together with the wide laminectomy necessary to expose it, weakened his spine sufficiently to cause dislocation.

Correction of the dislocation and fusion have made him a useful and active person with no great handicaps. It is probable that the tumor will recur, but it may not be for some years.

CASE 3.—C. F. B., a man aged 62, was admitted to the Massachusetts General Hospital on Jan. 18, 1937.

In 1912 the patient fell from the roof of a house, landing on a concrete floor. He was laid up for two weeks with a lame back and left flank. He was bothered off and on for a year by pain in the back. In 1933 he fell 25 feet (7.6 meters), landing on his back. He was unable to stand immediately after the accident, was in bed eight weeks and returned to his work as a carpenter several weeks later. No roentgenograms were taken at this time.

In the spring of 1935 he had pain in his left foot, thought to be from fallen arches.

In November he noticed pain in his left leg and in his back. This increased and was accompanied by weakness beginning in the left leg and later spreading to the right leg. There was no rectal or vesical disturbance. The weakness and pain increased, and when admitted he could barely stand alone.

Physical examination revealed no abnormality except as follows: The lumbar portion of the spine was flat and stiff. There was tenderness of all the lumbar spinous processes. The muscles of the lower parts of both legs were weak, somewhat atrophic and flabby. The quadriceps muscles were of good strength. Sensation was normal everywhere. Knee and ankle jerks were not obtained. Plantar response was down. A lumbar puncture showed evidence of dynamic block and a total protein of 1,380 mg. per hundred cubic centimeters. Roentgen examination showed areas of bone destruction in the second lumbar vertebra. Roentgenograms taken after the injection of iodized poppyseed oil showed a cap at the first lumbar vertebra.

Laminectomy was performed on March 17. A soft, reddish tumor mass was found lying in front of the dura and apparently arising in the body of the second lumbar vertebra. It was removed, and a large mass of tumor tissue was scooped out of the vertebral body, leaving a mere shell.

Pathologic examination showed that the tumor was a typical chordoma.

It was felt that a fusion operation was advisable and that roentgen therapy should be carried out.

On April 22, a fusion operation was performed by Dr. William A. Rogers. During convalescence from this operation intensive roentgen therapy was instituted. There was marked tanning of the skin of the back, and a small sinus developed which seemed to run down to the bone graft.

The improvement in the patient's neurologic condition was marked. His pain ceased at once, and the strength in his legs came back gradually.

The sinus has persisted but gives him little trouble and no discomfort.

Examination in March 1940, showed that his back was stiff and severely tanned by irradiation and the presence of the sinus mentioned above. His legs were strong; there was no sensory disturbance anywhere and the reflexes were normal.

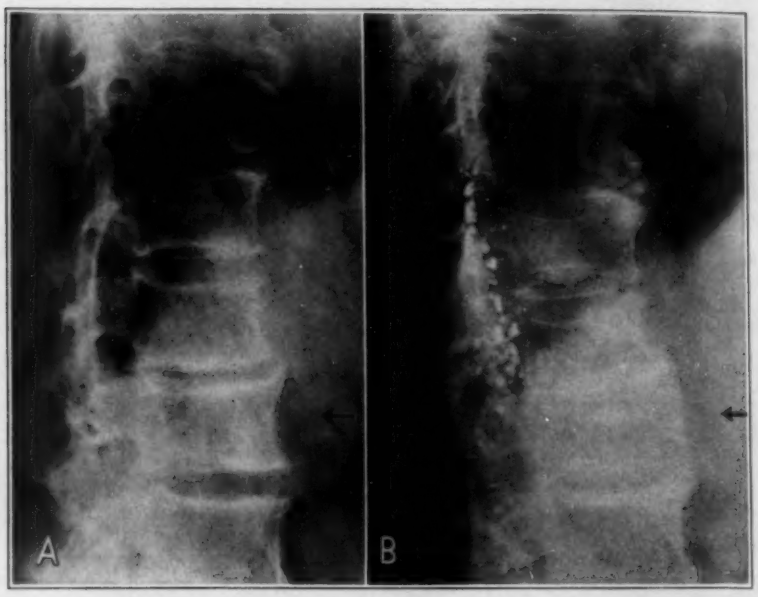

Fig. 7 (case 3).—*A*, condition before operation. Note the slight enlargement of the vertebral body and the mottled appearance. *B*, present condition. Note that the vertebral body shows more enlargement and more mottling. Note also the presence of the graft and the straight spine.

Roentgen examination shows increased destruction of the vertebral body at present, but there is no collapse and the spine is straight.

This patient has been put back on his feet and is leading a useful and happy life working as a carpenter. His back gives him no trouble whatever, aside from a tiny dressing over the sinus.

It was felt at the time of his operation that there was great danger of collapse of the shell of the vertebral body.

It is evident that the disease is progressing and will ultimately cause his death. The fusion and possibly roentgen therapy have increased his usefulness and life expectancy.

SUMMARY

The results of treatment of spinal and sacrococcygeal chordoma have been unsatisfactory.

A method of dealing with suitable sacrococcygeal chordomas by a two stage block resection is described.

The value of fusion after palliative removal of vertebral chordoma is pointed out.

Three hitherto unreported cases of chordoma illustrating these points are reported.

In the preparation of this study, Dr. Samuel Lowis made a careful study of the cases reported in the literature.

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SOLITARY NONPARASITIC CYSTS OF THE LIVER IN CHILDREN

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Solitary nonparasitic cysts of the liver are rare, especially in children. In only 25 of the 108 cases reported to date [1] did the lesion occur in children under 13 years of age.

Stoesser and Wangensteen [1a] in 1929 and Wikle and Charache [1b] in 1936 reviewed the literature in detail and reported cases of their own. Little has been added to knowledge concerning these cysts since then. Because the 2 children with this rare condition that have come under my observation exhibited some unusual features, I have thought it worth while to report their cases and to comment on the subject.

REPORT OF CASES

CASE 1.—C. D., a white girl aged 6 years, of Irish parentage, was admitted to the Children's Memorial Hospital on Oct. 31, 1935 because of a large, flabby abdomen and an abdominal tumor, both of which had been present since birth. When the child was born the tumor mass was described as firm but movable and about the size of an orange. It was located in the right upper quadrant. The skin of the abdomen at that time was flabby and wrinkled. As the child developed, the size of the mass remained unchanged, but the abdomen had become more pendulous and flabby, without much muscle tone (fig. 1). The birth history, past development and family history were essentially irrelevant. There had been no complaints referable to any system.

Physical Examination (Positive Findings Only).—The cephalic portion of the chest appeared flattened and narrow in its anteroposterior diameter. Below the level of the fifth ribs anteriorly there was a definite Harrison's groove, with marked flaring of the ribs on both sides. Inspection of the abdomen with the child lying flat on her back revealed a sunken, somewhat wrinkled skin with a noticeable linear wrinkle down the midline. The umbilicus was definitely to the left of the midline. The left flank had a normal contour, but the right flank seemed to have no muscle tone and bulged laterally. The superficial veins of the abdomen were prominent and appeared to sink into the subcutaneous tissue. With anterior flexion of the head on the neck, there was a visible contraction of both rectus abdominis muscles, the left being more prominent than the right. Both appeared hypoplastic. There was retraction of the upper, middle and lower

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From the Surgical and Pathologic Services of the Children's Memorial Hospital.

1. (*a*) Stoesser, A. V., and Wangensteen, O. H.: Solitary Nonparasitic Cysts of the Liver, Am. J. Dis. Child. **38**:241 (Aug.) 1929. (*b*) Wikle, H. T., and Charache, H.: Am. J. Surg. **31**:345, 1936.

segments of the left rectus muscle when the skin in that region was stimulated, but no response was seen on the right to a similar stimulation. The oblique muscles of the abdomen appeared normal on both sides.

The abdomen was flabby and doughy, and its contents were easily palpable. In the right upper quadrant, situated well under the ribs, was a firm, hard, round mass approximately 7 cm. in diameter. The tumor was freely movable and fell into the false pelvis when the child was erect.

When the child stood there was a falling forward of the abdomen in a pendulous, atonic protuberance, strongly suggesting the appearance of a postpartum abdomen in a multiparous woman.

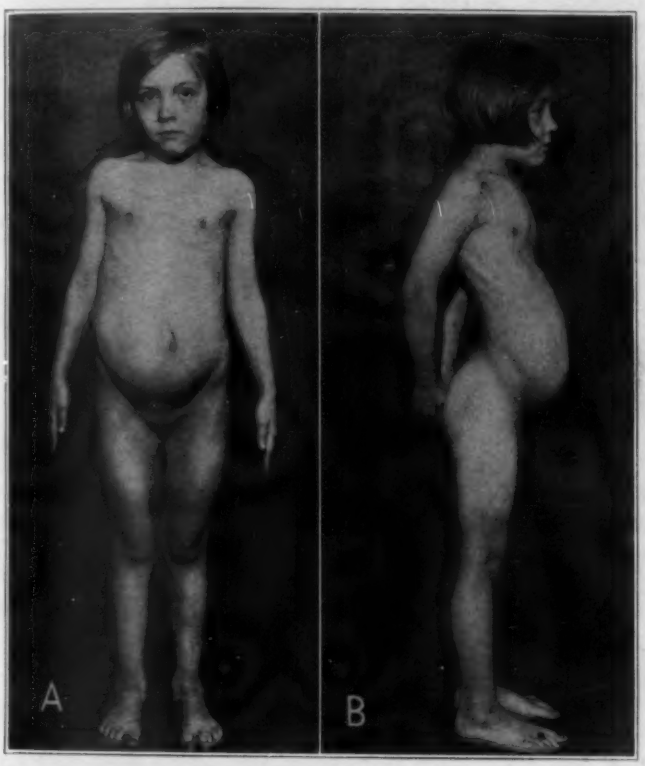

Fig. 1.—*A*, front view of the child before operation. Note the position of the unbilicus and the bulging of the right flank. *B*, lateral view. Note the well marked Harrison's groove.

There were no other positive physical findings of note. After making pyelograms and roentgen studies of the gastrointestinal tract (fig. 2), Dr. W. E. Anspach, the roentegenologist, summarized his data as follows:

1. A tumor mass 8.4 by 7.4 cm. was present in the right upper quadrant, having a fairly dense calcified material in its wall. It was not intimately associated with the colon. It was probably a calcified cyst.

2. There was no evidence of spina bifida.

3. There was slight dilatation of the renal pelvis, the calices and the ureters on both sides, somewhat more on the right than on the left. There was poor concentration of dye in the bladder.

Laboratory Studies.—The following values were obtained: hemoglobin (Sahli), 90 per cent; red blood cells, 4,300,000 per cubic millimeter; white blood cells, 10,000 per cubic millimeter; polymorphonuclears, 48 per cent; lymphocytes, 48 per cent, and eosinophils, 4 per cent. Repeated urinalyses revealed only an occasional leukocyte and epithelial cell. The Wassermann reaction was negative.

The preoperative diagnoses on November 2 were: (1) Congenital hypoplasia of the ventral abdominal musculature; (2) congenital calcified cystic abdominal tumor (gallbladder? teratoma?), and (3) mild right hydronephrosis (pressure from tumor mass).

Fig. 2.—*A*, anteroposterior roentgenogram of the tumor mass, showing its relation to the colon. *B*, lateral view, showing the relation of the tumor to the spine.

Operation.—On November 2 the abdomen was opened through a right upper rectus incision with the child under ethylene and ether anesthesia. The abdominal wall was abnormally relaxed, and the right rectus muscle was very thin and markedly diminished in size. When the abdominal cavity was entered, an aneurysm-like mass about 10 cm. in diameter was found lying just underneath the liver (fig. 3) and to the right of the gallbladder, which was pendulous, elongated and distended with bile, measuring approximately 14 cm. in length. The mass, which was attached to the relaxed round ligament of the liver by a thin, tough, fibrous pedicle, was rough and wrinkled, having the consistency of a hard rubber ball. It was covered with many dilated and tortuous veins. After the pedicle had been ligated with chromic catgut, the tumor mass was removed in toto, and the abdomen was closed in the usual manner, without drainage. The child's condition was good at the end of the operation.

Her postoperative course was uneventful, and renal functional tests revealed no abnormality. She was discharged home in good condition on November 18. When last seen in the outpatient department, on Nov. 16, 1938, the child seemed to be entirely well and without symptoms, although the abdomen was still sagging and required support.

Gross Description of Tumor Mass.—The specimen weighed 235 Gm., was oval and measured 8.5 cm. in its largest diameter and 7 cm. in width. The anterior, or presenting, surface (fig. 4 *A*) was thrown into a rich convolutional pattern, greatly resembling in this respect the surface of a normal brain, or a "Parisian coiffure." The posterior surface, or under surface, tended to be smooth. Transversing it were several flattened, tortuous vessels, which evidently entered into the formation of the vascular stalk by which the mass was suspended beneath the liver. When sectioned (fig. 4 *B*) the mass was seen to be composed of three distinct layers. The outer layer, of thick wavy folds, determined its external appearance. It was of fleshlike consistency, was pink to gray and measured 0.5 to 1 cm. in depth. On cross section this stratum consisted of fairly dense pink

Fig. 3.—Photograph of artist's drawing showing the position and appearance of the cyst at the time of operation. Note the pedicle.

connective tissue covered over by a thin, shiny capsule closely adherent to the fluted rolls and dips. In places a fine red stippling suggested the presence of blood vessels that had been transected.

A distinct cleavage plane separated it from the middle layer, which was responsible for the gross shape and outline. This was a dense, white, fairly rigid calcified shell about 2 mm. in thickness. It resembled a fetal skull in appearance and resiliency. From its inner surface, around the entire circumference and filling the largest part of the enclosed space, there projected a fine, friable, coral-like, papilliferous light brown growth. Its exquisite design suggested that it was composed of some type of delicate organized tissue. An aqueous medium of about 30 cm. of dark brown cloudy fluid filled its interstices and occupied the core. This fluid had a positive benzidine reaction for blood and contained no recognizable cytologic elements. The lining vaguely resembled marine flora. At one end of the bisected mass a tough fibrous partition passing across from side to side divided the mass into two unequal portions. The larger one conformed to the foregoing description. The small compartment, like a magnified

operculum of a trematode ovum (fig. 5), contained a denser yet more friable homogeneous material of idential color and without recognizable structure. The tumor mass was less dense than water.

Microscopic Description (Hematoxylin and Eosin, Mallory's Aniline Blue and Verhoeff's Elastic Tissue Stains).—The wall of the cyst was made up of three distinct layers, the outer of which was composed of loose fibrous tissue containing

Fig. 4.—*A*, external surface of the cyst, showing its resemblance to a fetal brain or a "Parisian coiffure." *B*, bisected cyst, revealing its three distinct layers. Note the inner calcified layer.

many large and small dilated engorged blood vessels, mainly veins which varied from 2 to 5 mm. in thickness. In focal places small clumps of irregularly arranged regions of liver cells (fig. 6) were seen. No other tissue was recognizable, and there was no increase in the elastic fibers. The outermost layer of tissue was thin and fibrous.

The middle layer was composed entirely of homogeneous, dense calcified material having an average thickness of 1 mm. It was not intimately bound to either the outer or the inner layers. In a few places blood vessels were enclosed in its structure.

The innermost layer was composed of a somewhat uniformly dense, homogeneous material which stained poorly. Here and there were clumps of partially disintegrated cells which could not be identified but resembled an old blood clot.

The final diagnosis was calcified pedunculated cyst of the liver.

CASE 2.—M. T., a white girl aged 6 months, was brought to the Children's Memorial Hospital on Sept. 6, 1933 by her mother, who had noticed for several months that the child's abdomen had become abnormally large. In every other way the child had been healthy and normal since birth.

Physical Examination.—The baby appeared bright and active and, except for the abdomen, seemed to be of normal development. Examination of the head,

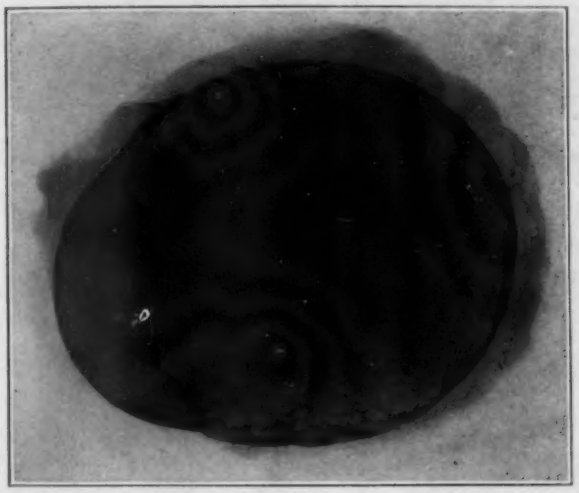

Fig. 5.—Roentgenogram of the surgically removed tumor. Note the resemblance to a trematode ovum.

neck and extremities revealed no abnormality. The abdomen was tremendously enlarged. The greatest circumference, which was 5 cm. above the umbilicus, was 53 cm. while the thoracic circumference at the level of the nipples was only 38 cm. The superficial veins were prominent on the abdominal wall, and the skin was tense and shiny. Palpation disclosed a cystlike mass on the right, extending from the costal margin down to Poupart's ligament and medially to the midline. It did not seem to be movable in any direction. On percussion the mass sounded dull, while the rest of the abdomen was very tympanitic. There was no tenderness over the tumor mass or elsewhere. The chest appeared to be shortened longitudinally, with some flaring of the lower ribs. The distance from the apex to the ninth rib was 4 inches (10 cm.). The breath sounds were suppressed over the base of the lung. The heart was evidently displaced to the left, as the right border was to the right of the sternum and the apex beat was 5 cm. to the left of the nipple line.

Roentgenograms made after intravenous injection of a dye showed nothing abnormal in the urinary tract.

The preoperative diagnosis was omental or mesenteric cyst.

Operation.—On September 9, with the child under ether anesthesia, the abdomen was opened by an upper right rectus incision. This disclosed a large, thick-walled cyst attached to the under surface of the liver but not adherent to any other abdominal viscera. After aspiration of 1½ liters of greenish fluid it was evident that the cyst could not be completely removed, because its superior surface formed the inferior capsule of the liver. A large part of the cyst was

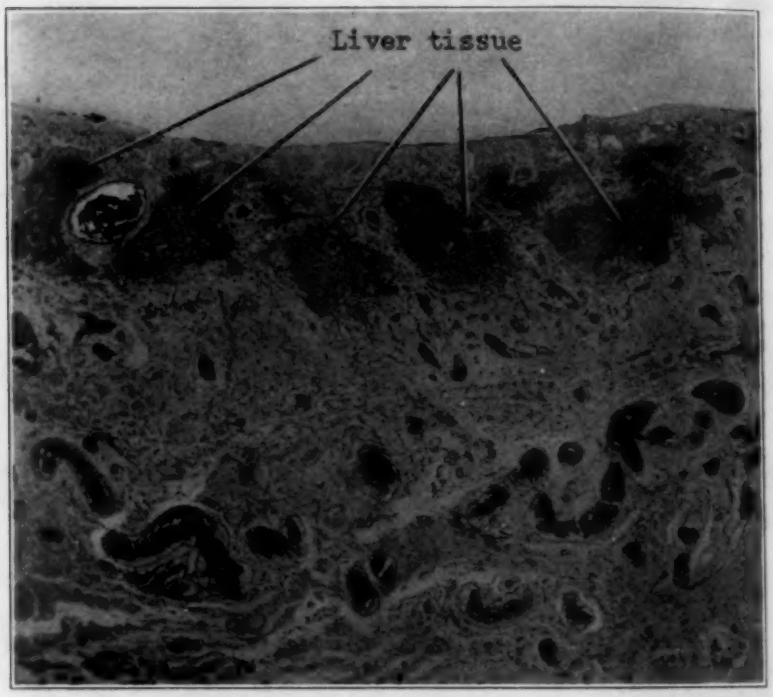

Fig. 6.—Photomicrograph (hematoxylin and eosin, × 30) showing clumps of liver cells in the outer layer of the cyst.

removed, and the remainder was marsupialized to the peritoneum of the abdominal wall. The cyst cavity was packed with iodoform gauze and the abdominal wound closed about it.

The cyst fluid on examination showed a cell count of 4,230, a specific gravity of 1.010 and no evidence of bile.

Subsequent History.—The abdominal wound healed kindly, and for several months the cyst cavity was packed repeatedly with iodoform gauze. As films taken of the cyst after injection of iodized poppyseed oil showed little reduction in the size of the cavity and it was becoming very difficult to insert the gauze packing, various sclerosing substances, such as tincture of iodine and silver nitrate solutions, were applied to the lining of the cyst, without any appreciable

effect. Two years after the first operation another exploration of the abdomen was made through the scar of the first operation. The cyst cavity was found to be much reduced in size but still irremovable from the under surface of the liver. The cavity was swabbed with phenol and alcohol, and marsupialization was reestablished. Profuse drainage from the cyst went on as before.

As roentgenograms made in August 1937 after injection of iodized poppyseed oil showed little diminution of the cyst, a sufficient quantity of Zenker's solution was injected to fill the cavity. At first this caused abdominal discomfort for several hours, but after weekly injections the pain gradually lessened. The amount of Zenker's solution that could be injected slowly decreased until September 1939, when the sinus closed. It has remained closed to the present date.

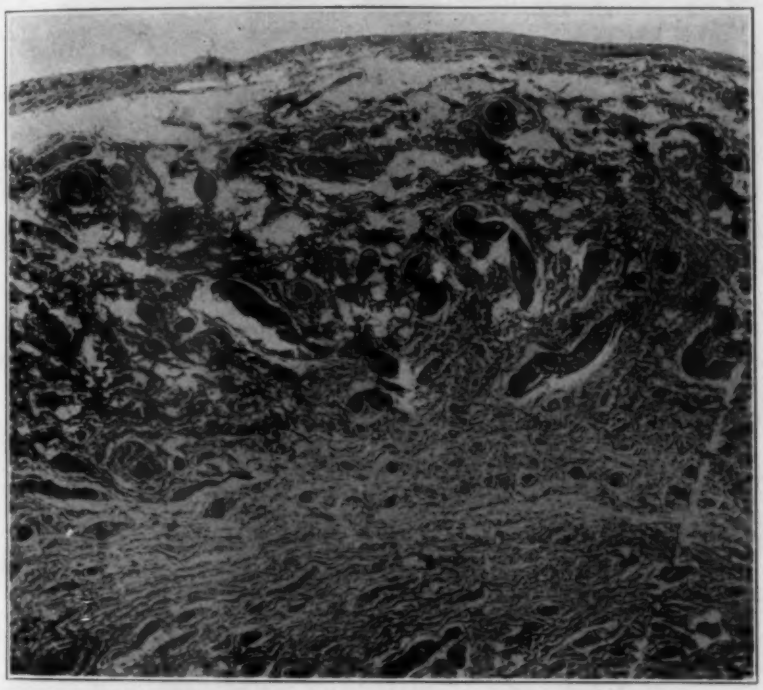

Fig. 7.—Photomicrograph (Mallory's aniline blue stain, × 30) showing the outermost layer of the cyst, with loose connective tissue and many engorged blood vessels.

Microscopic Description.—The cyst wall consisted essentially of three layers (fig. 8). The inner layer was the lining epithelium; the middle layer consisted of loose connective tissue and the outer layer of liver tissue.

The inner lining of the cyst was formed by a well preserved layer of stratified epithelium (fig. 9). The basal cells of this epithelium were polyhedral, with their nuclei arranged at right angles to the surface. The more superficial cells were elongated, flattened in a direction parallel to the surface. The epithelial layer was three to five cells deep, with nuclei which were in many respects similar to those of the liver or bile duct cells. The superficial cells had undergone moderate

degenerative changes. The basement membrane of the epithelium was not distinct, but there was no proliferation of epithelial elements into the cyst wall.

The next layer of the cyst wall was formed by more or less cellular collagenous fibrous tissue. The fibers and cells were arranged parallel to the surface. In a few areas there was proliferation of young fibroblasts. Here and there loose foci of polymorphonuclear leukocytes, eosinophils and lymphocytes were encountered. Moderate numbers of small blood vessels were present in this layer. In an outward direction there was a gradual transition into a loose connective tissue, in which numerous fairly large blood vessels and endothelium-lined lymphatic channels were observed. A narrow capsule-like strip of dense fibrous tissue

Fig. 8.—Low power photomicrograph (× 35) of the entire wall of the cyst with its lining epithelium. The middle portion consists of loose connective tissue; the outer portion, of liver tissue and its capsule.

separated this layer of vessels and lymphatics from a bandlike zone of liver tissue (fig. 10). The liver cells were typical as regards size, shape, staining properties and the character of the nuclei. The cytoplasm was somewhat pale, and the cell borders were distinct. The cells were arranged in parallel cords at right angles to the surface. The sinusoids were, as a rule, compressed, but here and there empty endothelium-lined channels were observed between the cords of liver cells.

Along the inner border of the liver tissue bile ducts were observed at fairly regular intervals. These were lined with columnar epithelium and were sometimes mildly dilated but always empty. The layer in which the bile ducts were

seen was mildly infiltrated with lymphocytes, eosinophils and polymorphonuclear leukocytes. Toward the periphery, somewhat distended venules, clearly corresponding to central veins, were seen between the rows of liver cells. The outermost layer of the cyst was formed by a thin, compact layer of collagenous fibrous tissue, which corresponded to the liver capsule and was lined with flat endothelial cells.

The final diagnosis was nonparasitic cyst of the liver.

GENERAL CONSIDERATIONS

Solitary nonparasitic cysts of the liver occur at all ages from fetal to late adult life [2] but are found rarely in infants and young children.

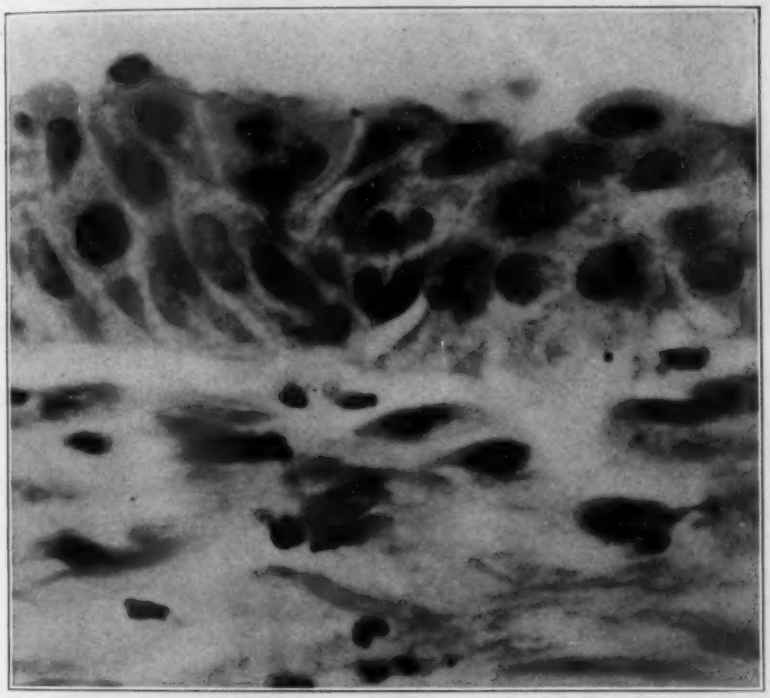

Fig. 9.—Photomicrograph (× 640). The cyst is lined by stratified epithelium, the surface cells of which have been altered by the pressure of the contents of the cyst.

Multiple cysts may occur in the liver alone but are most often associated with cystic disease of other organs or with congenital malformations. Cysts seem to occur more often in females than in males, the ratio being 4:1. This is explained on the basis that developmental defects are well known to be more common in the former sex.

Most cysts are located in the anteroinferior portions of the right lobe of the liver, but the left and quadrate lobes may be involved. In

2. Bland-Sutton, J.: Brit. M. J. **2**:1167, 1905.

a few cases the central part of the liver was the site of the cyst. The round ligament was involved in a few cases described by Harrington,[3] as it was in 1 of my cases (fig. 3). The amount of liver tissue displaced by these cysts is variable; sometimes the entire lobe is destroyed. Some cysts are microscopic, while others may fill almost the entire abdomen. Cysts of the liver grow very slowly if at all, and this in most cases accounts for the lack of signs and symptoms, as the adjacent organs adapt themselves to the presence of the tumor mass. Many

Fig. 10.—Photomicrograph (× 80). The peripheral portion of the cyst is covered by the capsule of the liver, beneath which there is well formed liver tissue.

of the large cysts are pedunculated and may show a marked degree of motility, as in my first case. When the pedicle is long, strangulation and hemorrhage may occur, and these two complications usually account for acute symptoms. Another characteristic of nonparasitic cysts is the low internal tension, the reverse being true of hydatid cysts, as has been recorded by Italian writers.

3. Harrington, S. W.: S. Clin. North America **6**:1191, 1926.

The external surface of these cysts is usually smooth, glistening and grayish blue, often showing many dilated veins and bands of tough fibrous tissue. The internal surface may be less regular and smooth, and the thickness of the wall is extremely variable. The contents of the cyst vary from a clear, watery, sometimes yellowish brown fluid, neutral or alkaline in reaction, to a semisolid material resembling an organizing blood clot. An analysis may show albumin, mucin, cholesterol, blood, hematoidin, hemosiderin, tyrosin, some granular and cellular debris and, rarely, bile. Some writers claim that the older cysts contain no bile because it is being constantly absorbed.

The microscopic appearance of the cyst wall usually demonstrates that it consists of three fairly distinct layers, an inner layer of loose tissue rich in ill defined cellular debris, a circular dense middle layer, poor in cell nuclei, containing a few blood vessels with thickened intima, and a loose outer layer rich in blood vessels, elastic fibers, muscle fibers, clumps of bile ducts and liver cells, covered with a thin fibrous capsule.

Various classifications of nonparasitic cysts of the liver have been attempted, but Sonntag's [4] is the one generally accepted: (1) blood cysts and degenerated cysts, (2) dermoid cysts, (3) lymphatic cysts due to obstruction or congenital dilatation of the lymphatics, (4) endothelial cysts, (5) cysts due to obstruction of bile ducts and (6) proliferative cysts (cystadenomas).

The possible mode of origin of these cysts has been discussed in detail by Bland-Sutton,[2] Moschcowitz,[5] Kaufmann [6] and Ewing.[7]

From all the theories expressed one must conclude that nonparasitic cysts of the liver are congenital and are of biliary origin, perhaps arising from aberrant bile ducts which result in benign cystic adenomas.

Solitary nonparasitic cysts of the liver [8] are usually symptomless unless they become large enough to give pressure symptoms or are palpable. It has been stated [1b] that in most cases symptoms are not produced in childhood other than the presence of an abdominal mass

4. Sonntag, E.: Beitr. z. klin. Chir. **86**:327, 1913.

5. Moschcowitz, E.: Am. J. M. Sc. **131**:674, 1906.

6. Kaufmann, E.: Lehrbuch der speziellen pathologischen Anatomie, ed. 6, Berlin, G. Reimer, 1911, vol. 1, p. 608.

7. Ewing, J.: Neoplastic Diseases, ed. 3, Philadelphia, W. B. Saunders Company, 1928, p. 731.

8. Witzel, O.: Centralbl. f. Gynäk. **4**:561, 1880. Sänger, M., and Klopp, A.: Arch. f. Gynäk. **16**:415, 1880. Miller, G. B.: Am. J. Obst. **48**:182, 1903. Shaw, H. L. K., and Elting, A. W.: Arch. Pediat. **26**:818, 1909. Lowenburg, H.: ibid. **35**:285, 1918. Everidge, J.: Lancet **1**:1748, 1914. Alexander, C. R.: Edinburgh M. J. **32**:61, 1925. Scalone, I.: Policlinico (sez. chir.) **31**:260, 1927. Eliason, E. L.: Ann. Surg. **99**:691, 1934. White, M.: Arch. Dis. Childhood **11**:319, 1936. Bagot, W. S.: Dublin J. M. Sc. **93**:265, 1892. Rolleston, H. D., and Kantback, A. A.: Virchows Arch. f. path. Anat. **130**:488, 1892.

in the right upper quadrant. When symptoms occur they are usually nausea, vomiting, diarrhea, pain in the upper part of the abdomen and, rarely, jaundice. The correct diagnosis of such cysts of the liver is difficult, being made only at operation or at autopsy. Roentgen examination of the abdomen may show the tumor to be a part of the liver shadow, and Hofmann (cited by Stoesser and Wangensteen [18]) brought out the differential points of such an examination. It was suspected in my first case that the tumor was attached to or associated with the gallbladder. With large pedunculated cysts the motility may be in all directions, the downward motion, however, being limited by the attachment to the liver. Pneumoperitoneum as a diagnostic aid has been disappointing, but direct visualization of the tumor with the peritoneoscope may be of diagnostic help.

Surgical removal as done in my first case is the treatment of choice when possible. Complete extirpation cannot always be done, however, and drainage and marsupialization as done in my second case may be the procedure of necessity. Fatalities have been reported due to shock from the sudden release of intra-abdominal pressure. This can be avoided by the injection of epinephrine hydrochloride subcutaneously before the cyst is opened and by slow removal of the fluid. This may also prevent complete evisceration, which has been observed by some surgeons, especially in treating these cysts in children. The prognosis in general is good if the patient survives operation, but the operative mortality of nonparasitic cystic disease of the liver in the reported cases varies between 10 and 30 per cent.

COMMENT

From the description of my 2 cases it is quite evident that both cysts were congenital. In case 1 the tumor was present at birth and was associated with congenital weakness and atrophy of some of the muscles of the abdominal wall, and in case 2 it was discovered a few months after birth.

As liver tissue was observed in the walls of both cysts, it is fair to assume from that fact and from their location that the cysts originated in connection with the liver. The first case is unique in its bizarre roentgen and gross appearance. A review of the literature fails to show a similar case. Because liver cells were observed in the outer layer of the cyst, I believe that this tumor mass was originally an accessory lobe of the liver and that during the intrauterine period, when the abdominal contents were returned to the abdomen and rotating to assume their normal position, this mass of liver tissue became twisted on its pedicle, producing necrosis of its central portion from loss of blood supply. This was followed by the deposition of calcium in its middle portion. Subsequently the tumor mass failed to increase in size

owing to faulty blood supply and failed to give symptoms because of its location and attachment. In short, I believe that this was a congenital nonparasitic calcified cyst of an accessory lobe of the liver.

In the second case the presence of compressed liver cells in the lining of the cysts would seem to indicate that the cyst arose from obstruction of the biliary ducts near the inferior capsule of the liver, producing a cystadenoma of the liver.

CONCLUSION

Two congenital nonparasitic cysts of the liver in children are presented. In 1 case the calcification and bizarre appearance of the cyst are pointed out. The use of Zenker's solution as a sclerosing agent in the obliteration of these cysts is suggested.

Dr. W. Price Killingsworth, of Port Arthur, Texas, assisted in describing the pathologic specimens.

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CHANGES IN BONES AND JOINTS RESULTING FROM INTERRUPTION OF CIRCULATION

I. GENERAL CONSIDERATIONS AND CHANGES RESULTING FROM INJURIES

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CHICAGO

Lesions of various organs resulting from interruption of the circulation are of common occurrence, and their pathologic and clinical aspects are generally known to the members of the medical profession. Examples are occlusions of the coronary, cerebral and pulmonary arteries and infarctions of the kidney and of the spleen. However, in the case of bones the same generalizations cannot be made. Although it has been accepted since the report of Langer [1] in 1875 that the bones contain end arteries, knowledge of changes in bones and joints from vascular blockage was slow in developing. There are a number of reasons for this: first, the absence or mildness of immediate symptoms resulting from simple interruption of circulation in bone; second, postmortem examinations of the skeleton are much less common and less extensive than are those of the viscera; third, operation affording a chance for pathologic examination is seldom indicated with most forms of aseptic bone necrosis, and fourth, certain roentgen signs of this condition which are late in appearing were long confused with those of other chronic lesions.

Septic embolism of bones has long been regarded as one of the causes of pyogenic and tuberculous osteomyelitis, but definite information on this point is scanty. Volkmann [2] in 1864 reported multiple suppurating infarcts of bones in a case of septic endocarditis in which necropsy was performed. There is a difference of opinion as to the role of vascular blockage in the pathogenesis of the usual hematogenous osteomyelitis, whether it arises from the activity of bacteria which lodge in the tissues and sinusoids of the bone or from that of organisms contained in small emboli which block end arterioles of the metaphysial

From the Department of Surgery of the University of Chicago.

1. von Langer, C.: Ueber das Gefäss-system der Röhrenknochen, mit Beiträgen zur Kenntnis des Baues und der Entwickelung des Knochengewebes, Vienna, K. Gerolds Sohn, 1875.

2. Volkmann, R.: Embolische Knochennekrose nach Endocarditis, Arch. f. klin. Chir. **5**:330, 1864.

regions. Information is difficult to obtain, because in either case the initial lesion is small and is rapidly obscured by spread of the inflammation to surrounding tissues. That a large artery may be blocked by a septic embolus resulting in massive bone necrosis with slow secondary infection and resolution of the necrotic area has been claimed by Axhausen. Such an occurrence would necessitate the existence of a septic focus in the pulmonary veins, the left side of the heart or the arteries, giving rise to the embolus, as particles passing through the lungs would be too small to produce the obstruction. König [3] expressed the belief which has been extensively accepted, that areas of necrosis associated with tuberculosis of the metaphyses and epiphyses, some of which are wedge shaped, are the result of embolism of caseous tuberculous material gaining entrance to the arterial circulation from tuberculous lungs by way of the pulmonary veins. While the theory is very plausible, direct proof is still lacking.

Knowledge of simple or aseptic interruption of the circulation in bone has been developed mainly during the past thirty years, owing in large part to the contributions of Axhausen, who, together with Bergmann,[4] has recently published a very comprehensive review and extensive bibliography of the subject. However, since then there have been other reports which have added considerably to knowledge of the subject.

The first information on the effect of aseptic interruption of the circulation in bone was obtained by a study of transplanted bone. Ollier expressed the opinion that the entire transplant remains alive, becomes attached to the bone and subsequently undergoes more or less transformation in adjusting to its location and function. Barth [5] was the first to recognize that the bone tissue dies and later is invaded and replaced by new bone. He expressed the opinion that there is death of the entire transplant and that new bone grows into it from the bone into which it was transplanted. Axhausen first demonstrated that the periosteum and endosteum of the transplant survive and take the most active part in generating new bone which replaces the dead bone.[4] But in case the transplant is extensively and snugly embedded in bone the invasion and replacement may be in large part by tissue from the surrounding bone. Cornil and Coudray [6] demonstrated that with frac-

3. König, F.: Die specielle Tuberculose der Knochen und Gelenke, Berlin, August Hirschwald, 1896.

4. Axhausen, G., and Bergmann, E.: Die Ernährungsunterbrechungen am Knochen, in Henke, F., and Lubarsh, O.: Handbuch der speziellen pathologischen Anatomie und Histologie, Berlin, Julius Springer, 1937, vol. 9, pt. 3.

5. Barth: Ueber histologische Befunde nach Knochenimplantation, Arch. f. klin. Chir. **46**:409, 1893.

6. Cornil and Coudray: Du cal au point de vue expérimental et histologique, J. de l'anat. et physiol. **50**:103, 1904.

tures in rabbits there is necrosis of the cortex for a short distance back from the fracture line, with subsequent creeping replacement of the dead bone by new bone. Lexer [7] performed homotransplantations of joints, with the result that after successful union and transformation of the bone the articulation gradually broke down, with marked impairment of function.

Aseptic necrosis developing in bone that has not been transplanted was recognized first in lesions of the epiphyses and short bones both in children and in adults. Lesions situated in the shaft have only recently been recognized. The epiphysial disturbances designated as Legg-Perthes disease, Köhler's disease of the metatarsal bone, Osgood-Schlatter disease and Kienböck's lunatum and Köhler's tarsal navicular diseases were gradually identified by pathologic examinations as necrosing lesions. It was learned simultaneously that certain fractures bordering on joints and dislocations may cut off blood supply and cause necrosis of the end of the bone. Axhausen observed a case in which rather recent anemic infarcts of the bones of an adult were present, some of which were in the epiphyses and others in the metaphyses, which he considered due to embolism. Kahlstrom, Burton and I [8] were the first to report cases of very extensive aseptic necrosis of both shafts and epiphyses of bones terminating in permanent large calcified infarcts in the shafts and in arthritis deformans wherever the necrosis bordered on a joint.

Pathologic and roentgen studies have revealed certain reactions of the surrounding living bone and joint structures to necrotic bone and necrotic cartilage resulting from aseptic interruption of the circulation. A reparative reaction is set up in the living bone about the dead area which bears some resemblance to fibrous callus formation in fracture healing. But removal of dead bone as well as formation of new bone must be accomplished in the process of repair. A zone of fibrous tissue forms in the marrow spaces of spongy bone or along the surface of compact bone about the necrotic focus. This fibrous tissue gradually invades the marrow spaces of the dead cancellous bone, breaking down and replacing the dead marrow. As the fibrous zone advances into the dead bone on the one side it becomes transformed into an advancing osteogenetic zone on the other. In this zone the fibrous tissue (i. e.,

7. Lexer, E.: Die freien Transplantationen, Stuttgart, Ferdinand Enke, 1924, pt. 2.

8. Kahlstrom, S. C.; Burton, C. C., and Phemister, D. B.: Aseptic Necrosis of Bone: I. Infarction of Bones in Caisson Disease Resulting in Encapsulated and Calcified Areas in Diaphyses and in Arthritis Deformans, Surg., Gynec. & Obst. **68**:129, 1939; II. Infarction of Bones of Undetermined Etiology Resulting in Encapsulated and Calcified Areas in Diaphyses and in Arthritis Deformans, ibid. **68**:631, 1939.

fibrous marrow) is transformed into bone, which is laid down on and gradually replaces the old dead bone, and into hemopoietic and fatty marrow. The dead bone is removed in part by osteoclasts and in part by the direct action of the new bone as it is being laid down, a process which has been called "creeping substitution." Necrotic cortex is invaded and replaced as in a transplant. These two processes of fibrous invasion and of metaplasia and replacement of the dead bone by new bone usually go hand in hand in a relatively narrow band (fig. 22). But in some cases the fibrous invasion may be far in advance of the zone of transformation, leaving a thick zone of dead bone filled with fibrous marrow. There is considerable variation in the rate of progress of the transformation and in the extent to which the dead bone is removed and replaced by new bone. These factors are influenced by age, size and location of the necrotic area, function, trauma and nonunion of fractures which may be present. Aseptic necrotic bone in children as in Legg-Perthes disease is nearly always completely replaced by new bone, and substitution proceeds more rapidly than in adults. Small necrotic areas continuous with living bone are usually completely replaced by new bone in the course of a few weeks or months. But the presence of an ununited fracture may greatly delay invasion and transformation, as in case 3.

Until recently it was the generally accepted view that the reparative impulse would last as long as dead bone persisted and that the necrotic area, regardless of size, was eventually all invaded and replaced by new bone. But the reports by Kahlstrom, Burton and me [8] and by me alone [9] have shown that in the case of adults large necrotic areas, especially in the shafts of bones but also in the head and condyles of the femur, may be incompletely removed. A possible factor in explanation of this may be that after a considerable part of the peripheral portion has been replaced the strength of the bone becomes sufficient for the function which it is called on to perform. The reparative stimulus is then greatly reduced or removed; the necrotic area remains stationary in size, and the fibrous zone of transformation about it may undergo more or less extensive calcification and ossification. There may also be calcification scattered throughout the necrotic portion inside the fibrous zone. These features are illustrated in femoral heads by figure 22 and in the shafts in the report by Kahlstrom, Burton and me.

Function hastens to some extent the rate and increases the extent of repair. It should, however, be limited well within the strength of the necrotic bone and of the newly forming bone during the major part of the period of creeping substitution. If in case of necrosis of the

9. Phemister, D. B.: Aseptische Knochennekrose bei Frakturen, Transplantationen und Gefässverschlüssen, Ztschr. f. orthop. Chir. **55**:161, 1931.

ends of the bones there is too much weight bearing, strain or trauma in any form, there will be fracture of the necrotic bone or of the weak new bone along the zone of substitution, with more or less collapse of the articular portion, erosion of the necrotic trabeculae from friction of fragments and, in some cases, the establishment of fibrous or fibrocartilaginous union or even of pseudarthrosis between the necrotic and the living portions. This is illustrated by case 9 (figs. 13 to 16). The bone meal created by the erosion may be driven into the cancellous spaces of the dead portion to some extent. The establishment of a line of nonunion may greatly retard invasion and replacement of the dead bone and increase the deformity of the joint (case 6). When there is necrosis of bone bordering on a joint there is always more or less secondary change in the articulation.

If there is collapse of the bone the articular cartilage is damaged. The nutrition of the cartilage is derived partly from the synovial fluid and partly from tissue fluid coming from the circulation of the underlying bone. During the period of growth the cartilage may get adequate nutrition from the synovial fluid alone and continue to grow, as is shown by the experiments of Nussbaum[10] in which the blood supply of the bone of the epiphysis was severed. Also, pathologic studies of the necrosing lesions of the epiphyses during the period of growth have shown that, while the cartilage may show evidences of nutritional disturbance in places, it in large part remains alive, becomes thicker than normal as in Legg-Perthes disease and after the necrotic bone is replaced takes part in further epiphysial growth.

However, in adults the articular cartilage is less dependent on synovial fluid for nutrition. This is perhaps related to the more fibrous and less penetrable character of the layer along its free surface. Consequently, interruption of the circulation in the bone of the epiphysis causes interference with the nutrition of the cartilage. This varies considerably in degree with the case. Usually it is quite obvious, and the cartilage cells, especially "deep in," gradually diminish in staining power. A striking fact is that if for a variable period (up to several months) there is invasion and creeping replacement of the underlying cortex by new bone, the new blood supply underneath the cartilage furnishes it with nutrition, and its cells largely regain their normal staining properties. Figuratively speaking, the cartilage is rescued from a state of hibernation during which it received only scant nutrition from the synovial fluid. This is illustrated by case 8 (figs. 24 and 25). One patient examined ten weeks and another examined twenty-two weeks after fracture of the

10. Nussbaum: Die arteriellen Gefässe der Epiphysen des Oberschenkels und ihre Beziehungen zu normalen und pathologischen Vorgängen, Beitr. z. klin. Chir. **130**:495, 1923.

neck of the femur with necrosis of the femoral head showed complete restoration of staining properties of the cartilage in the regions where underlying living bone had been restored, while that over the remaining dead area stained feebly. If, however, the replacement of the underlying bone by new bone is delayed for longer than nine to twelve months the cartilage is apt to die. Dead cartilage may remain for long periods, may be eroded in weight-bearing portions or may be replaced by fibrocartilage or even by bone if the underlying living bone is eventually restored.

In cases of long-standing involvement a chronic deforming arthritis is usually established, consisting of fibrillation and faulting of the fibrocartilage, marginal lipping, villous arthritis, osteocartilaginous loose bodies and, in cases of advanced involvement, disintegration and deformity of the articulation. The most important known factor in the production of the arthritis deformans is the necrotic articular cartilage, although eroded pieces of bone have been found at the center of the cartilaginous loose bodies in some cases. Axhausen [11] found that when cartilage of the knee joint of the dog was killed in situ by chemicals, heat or a high frequency electric current, the changes of arthritis deformans developed, involving the articular cartilage, the ends of the bone and the synovial lining. These changes are illustrated in case 10 and in the cases reported by Kahlstrom, Burton and me.

Roentgen studies have come to play an increasingly greater role in the recognition of the effects of circulatory blockage of the skeleton as they have been correlated with the pathologic observations in the bones and joints. Changes in density of the bone result from atrophy of disuse, from creeping replacement of dead bone by new bone, from pathologic fractures and collapse of the dead bone bordering on joints, from compression of dead trabeculae, from infiltration of bone sand into the dead marrow spaces and from calcification of the line of demarcation and the interior of old stationary necrotic areas located in the medullary and cancellous regions. In the case of joints they occur from calcification of cartilaginous loose bodies, marginal lipping, loss of articular cartilage and subchondral sclerosis in the later stages of arthritis deformans. Since time is required for the development of all of these changes, there are no demonstrable roentgen changes in the early stages of aseptic necrosis. In case the cause of necrosis is a fracture followed by nonunion resulting in marked disuse, there is enough atrophy of the adjacent living bone in one to two months to cause it to cast in roentgenograms a shadow fainter than that cast by the dead bone, which retains its original density. Fibrous tissue invasion of the dead bone causes no change in density, but creeping substitution by new bone alters density. If it takes place

11. Axhausen, G.: Neue Untersuchungen über die Rolle der Knorpelnekrose in der Pathogenese der Arthritis, Arch. f. klin. Chir. **104**:20, 1914.

in the presence of a considerable degree of disuse, as in a necrotic femoral head in a case of ununited fracture of the neck of the femur (case 8, fig. 24), the new bone is less dense than the old and casts a fainter shadow. In some of these cases central portions of the head may be replaced by fatty bone marrow, which gives the roentgen appearance of a cavity. If, however, there is little or no disuse, the new bone is laid down in greater amounts, and the density approximates the normal. But the shadows of the trabeculae are usually irregular, which may suggest the previous existence of a necrotic area. Flattening of the articular surface and fracture lines within or at the limits of the dense bone are important signs. Compression of trabeculae, especially in necrosing lesions in children, may give rise to some degree of increased density. Axhausen and Bergmann [4] have reported that the broken-down bone of a collapsed region may be so finely powdered that it works its way under pressure into the cancellous spaces of the remaining dead bone, causing it to cast shadows of increased density in roentgenograms. Weil, on the other hand, concluded that the amorphous material filling these cancellous spaces is disintegrated blood.[4] Examination of materials available for this report showed only relatively small amounts of eroded bone dust driven into the marrow spaces of the dead bone, probably not enough to increase materially its density in roentgenograms. Material resembling that shown in Axhausen's photomicrographs was seen, but it appeared to be mainly the debris of necrotic marrow and blood, as in figures 15*A* and 16*A*, with relatively slight infiltration of the dead bone by bone dust. The calcified and ossified line of demarcation which may develop about a stationary necrotic area in the cancellous bone or the medullary cavity of the shaft casts a definite shadow of increased density in roentgenograms (case 7). There may also be sufficient calcification within to cause the entire necrotic area to cast a more or less blotchy shadow of increased density, as in previously reported cases (case 8) and in others to appear in part II.

Causes.—The causes of interruption of circulation are in general less well understood in the case of bone than in the case of soft parts. The best known cause is injury of the blood vessels produced by fractures, dislocations and operations. For this reason the lesions resulting from injury will be considered first, and those due to other and little understood causes will be left for consideration in part II.

CHANGES RESULTING FROM INJURIES

Traumatic interruption of the circulation of bone is most frequently caused by fracture. In fact, there is a variable amount, usually small, of necrosis of fragment ends in almost every case of fracture, but it remains unrecognized and undergoes creeping substitution with the healing of the fracture. Extensive necrosis, which may impede the repair

of the injury and be diagnosed in roentgenograms, is most often seen with comminuted fractures and with fractures of the ends of certain bones and of short bones of the carpus and tarsus. Ransohoff [12] reported a case of fracture of the middle third of the shaft of the humerus followed by marked wavy reduction in density of the entire lower fragment, which he interpreted as due to injury of the nutrient artery followed by necrosis and repair. Ten years later a roentgenogram showed the appearance restored to normal.

Comminuted fractures. If the ends of the fragments are shattered, the broken-off pieces usually undergo partial to complete necrosis, but in some cases blood vessels passing by way of attached soft parts keep the circulation intact. The unossified periosteal and endosteal osteogenic elements of the splinter take part in callus formation if the splinter is not widely displaced from the fracture site. There is also invasion of the dead bone by blood vessels and osteogenic tissue, and creeping replacement of the dead bone by new bone is gradually accomplished, analogous to the changes in a transplant. If the splinter is widely displaced into soft parts it will slowly undergo absorption.[9] Usually the presence of necrotic bone in the splinters retards somewhat but does not greatly alter the course of healing if there are good alinement and fixation of the fracture. Lexer [7] and Axhausen and Bergmann [4] even claimed that necrotic bone at the site of fracture augments the stimulus for bony union. This is in contradiction to the general observation that the less the amount of necrotic tissue present the better any wound heals. The behavior of a large detached fragment as revealed by roentgenograms and biopsy is presented in the following case of fracture of the tibia with nonunion.

REPORT OF CASES

Case 1.—A man aged 55 fell 25 feet (7.6 meters), injuring the right leg. A roentgenogram taken immediately (fig. 1 *A*) revealed fractures of both bones of the lower third. The tibia was shattered, with a large displaced splinter and a line extending into the angle joint. At operation Steinmann pins were inserted through the os calcis and the upper end of the tibia and attached to a sterilized Roger Anderson reduction apparatus. The fracture was then cut down on, the fragments and splinter brought into good alinement, the wound closed and the extremity encased in plaster. Primary wound healing followed. The pins were removed in four weeks and the cast in fifteen weeks, at the end of which time there was motion at the site of fracture of the tibia. Roentgenograms (figs. 1 *B* and 1 *C*) then showed bony union of the fibula and nonunion of the tibia. The upper and lower tibial fragments were reduced in density, while the splinter (*x*) held its original density. These findings led to a diagnosis of injury of the blood supply and aseptic necrosis of the splinter. It was probably a causative factor in the nonunion. An onlay bone grafting operation was performed one hundred

12. Ransohoff, N. S.: Osteoporosis of the Humerus Following Fracture, Ann. Surg. **89**:571, 1929.

and twelve days after the injury, at which time the exposed splinter was found to be pale and not to bleed from the stripped cortical surface, while the upper and lower fragments were pink and there was slight bleeding when their surfaces were denuded. Biopsy of material from the splinter was done. Onlay cortical grafts taken from the shaft above were applied from the upper to the lower fragments posteriorly and mesially and from the upper fragment to the splinter laterally. Cancellous bone grafts were applied along the fracture lines anteriorly. Microscopic sections of the excised piece of splinter showed nearly

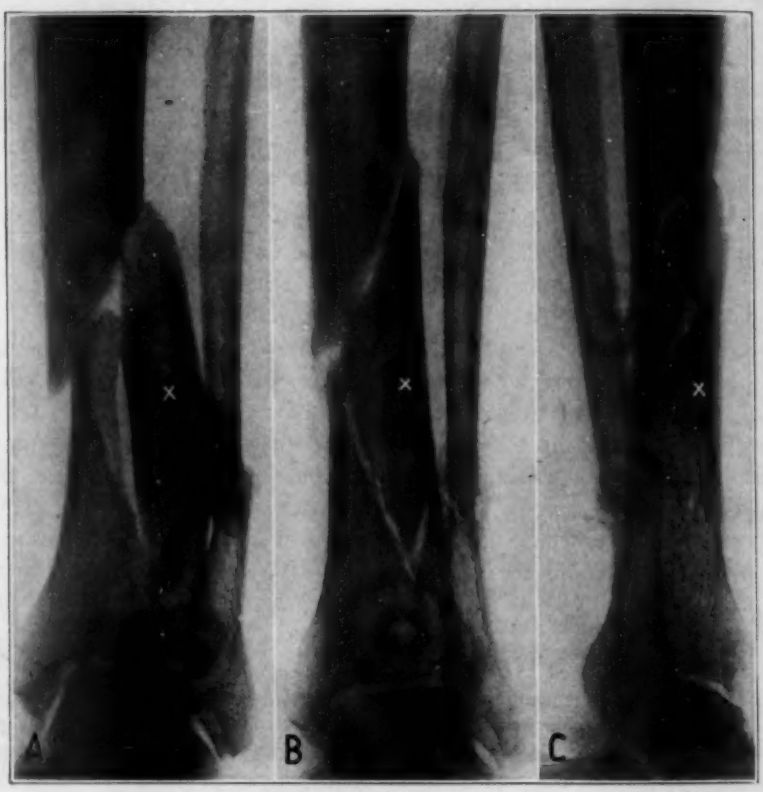

Fig. 1 (case 1).—The fragment (*x*) detached by the fracture became necrotic. *A*, fresh fracture before open reduction. *B* and *C*, condition one hundred and six days later. The fracture is ununited, and the necrotic fragment (*x*) is denser than the atrophied living fragments.

all of the lacunae devoid of cells, and where cells were present they stained poorly. There was a small amount of revascularization of canals and of creeping replacement of old cortex by new bone along the surface (fig. 2). Bony union followed, but roentgenograms showed the density of the splinter remaining about the same. The patient began walking eight months after injury. Ten months after injury (fig. 3, *A* and *B*) there was reduction of density in the lower portion of the splinter, indicating creeping replacement of the dead bone. Work was resumed

after about one and one-half years. Two and one-half years after the injury, roentgenograms (fig. 3, *C* and *D*) showed more or less uniformity of density and wavy lamellar shadows throughout the fragments, the grafts and the splinter, indicative of complete replacement of the necrotic bone. While no roentgenograms were taken after the tenth month until after the lapse of two and one-half years, it is safe to assume from the rate of progress to the tenth month that at least two years were required for renovation of the necrotic splinter. Other cases in

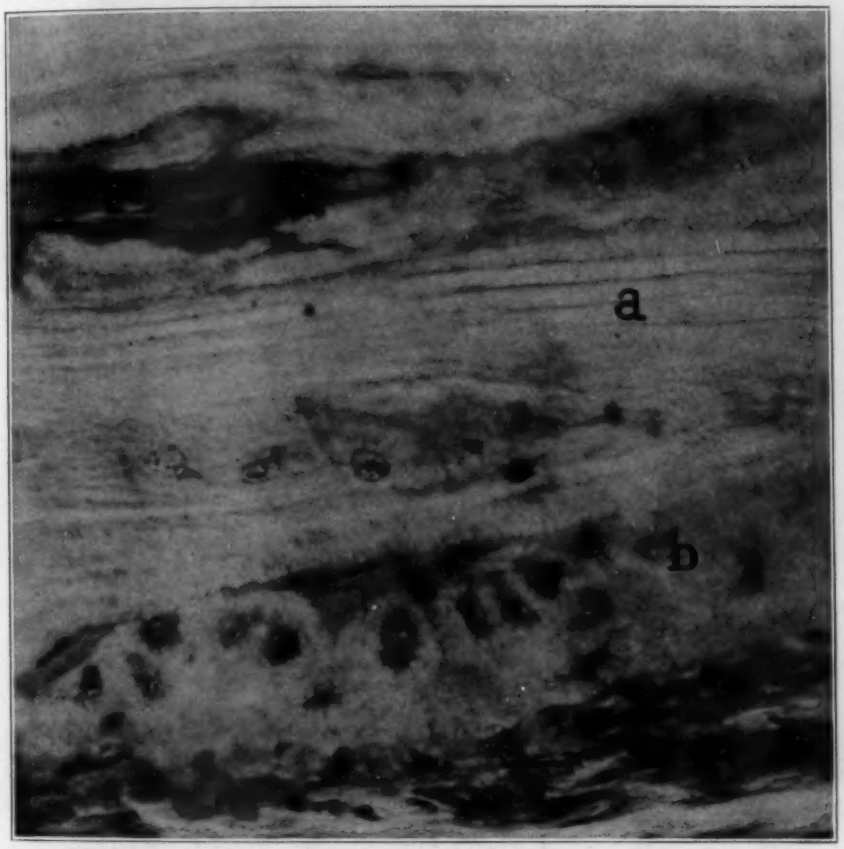

Fig. 2 (case 1).—Biopsy specimen of the fragment (*x*) one hundred and twelve days after injury, showing necrotic bone (*a*) and beginning creeping replacement by new bone (*b*).

which there were large splinters but in which no biopsy was performed have been followed with roentgenograms in which similar changes in density indicated necrosis of the splinter followed by creeping replacement by new bone.

There is sometimes a good deal of aseptic necrosis to be observed on microscopic examination of the ends of fragments resected at operation for ununited fracture, especially if they are of relatively short duration,

before creeping replacement has advanced very far. The condition can scarcely be diagnosed in roentgenograms because of the frequent changes in density produced by the overlapping periosteal and endosteal callus of the fragment ends. Tear of the nutrient artery in shaft fractures may cause excessive necrosis but, if so, it rarely alters the course of the fracture. Cases of regional osteoporosis following fracture of the type reported by Ransohoff [12] may result from nutrient artery injury. During

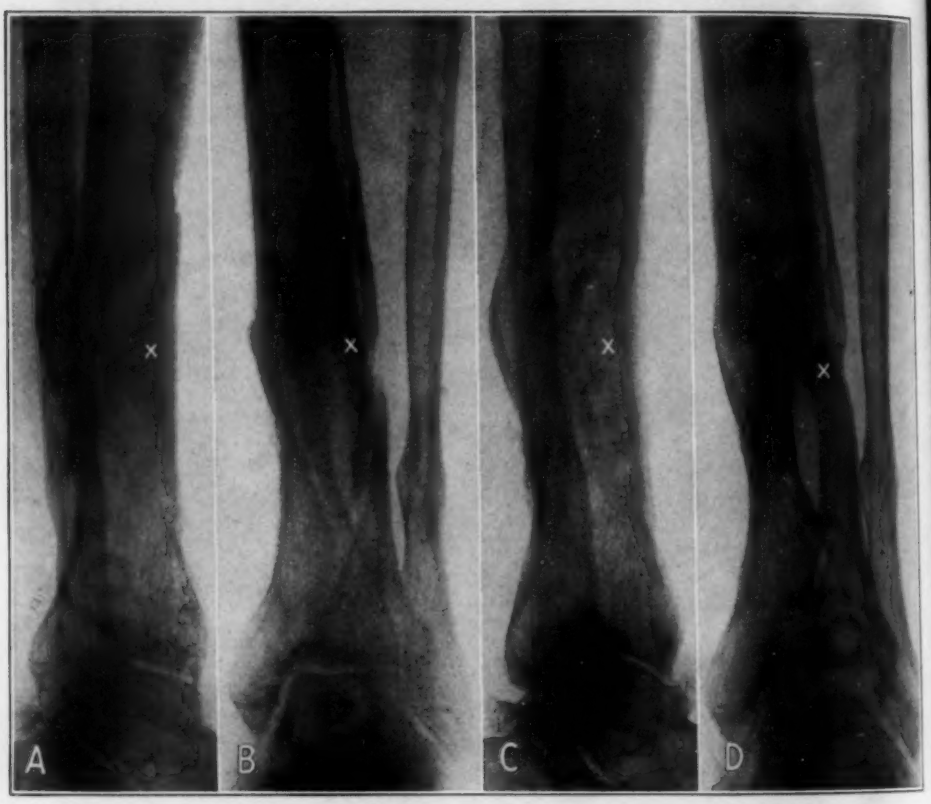

Fig. 3 (case 1).—*A* and *B*, condition ten months after injury. The fracture is united, and the dense necrotic fragment (*x*) has been partly replaced by less dense new bone in the lower portion. *C* and *D*, condition two and one-half years after fracture; the necrotic fragment has been replaced by wavy new bone.

operation for nonunion or malposition there is often extensive stripping of periosteum from the ends of the fragment. This appears to make little difference about healing if the operation is otherwise properly performed, and it is difficult to know whether or not the fragment ends have been devitalized. That devitalization may occur is demonstrated by the following case, in which it was found in a bulbous fragment at the fourth operation for nonunion.

CASE 2.—A man aged 53 had an ununited fracture of the lower end of the left femur of twenty-eight months' duration. Three attempts had been made by operation to obtain union, without success, the last one four and one-half months previously. There had been primary union of the wound each time. When the fragment ends were bared during a bone grafting operation, the bone of the lower fragment looked pink and viable, but the distal 4.5 cm. of the upper fragment, which was enlarged and sclerosed from bony callus, was pale and bloodless. Necrosis was diagnosed, and the end was resected through healthy-appearing bone. On longitudinal section the interior was sclerosed and pale to the same level (fig. 4). Microscopic sections revealed necrosis of bone throughout the entire area. There was a good deal of connective tissue invasion, and some dilatation of the cannular systems of the upper necrotic portion was present, but there was little evidence of creeping substitution by new bone. The necrosis had resulted secondarily and had probably followed the stripping of fragment at the last operation, as judged by the small amount of repair in it.

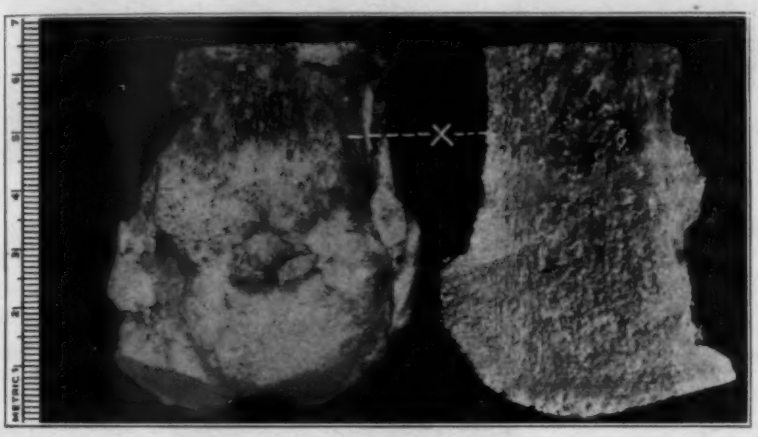

Fig. 4 (case 2).—Grayish white aseptic necrotic end (below *x*) of the upper fragment of an ununited fracture, resected at operation.

Necrosis of the body of the astragalus following fracture of the neck in 1 case (Dr. Dean Lewis) and fracture of the neck with posterior dislocation of the body in another case were previously reported on by me.[9] The diagnosis was based on roentgen evidences of persistence of the original density of the body in the presence of reduced density from atrophy of disuse in the surrounding living bone and of later progressive reduction of density due to creeping substitution. In 1 case there were also irregularity and flattening of the ankle joint surface of the astragalus.

An additional case is reported, in which the head was also necrotic (Dr. G. T. Aitken) and in which pathologic studies were made of the excised astragalus.

CASE 3.—A man aged 65 sustained a closed injury to the left ankle in which the neck of the astragalus was fractured and the body posteriorly dislocated (fig. 5 *A*). Reduction was accomplished by open operation. There were primary wound healing and prolonged immobilization in a cast, but the ankle remained weak and painful. Roentgenograms taken one year and nineteen days after injury (fig. 5, *B* and *C*) revealed the body of the astragalus in the normal position

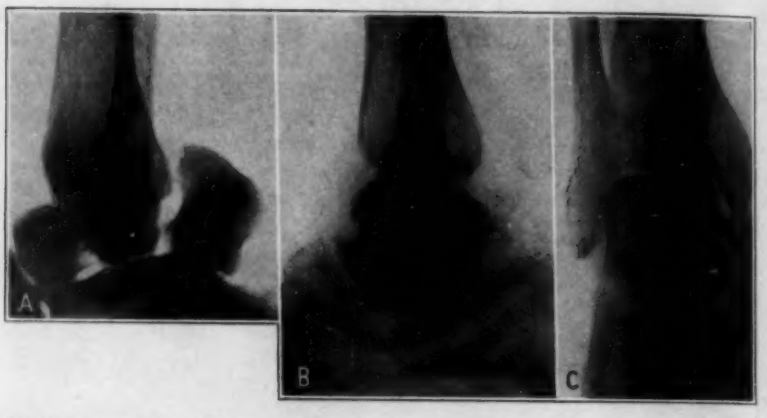

Fig. 5 (case 3).—*A*, fresh fracture of the neck of the astragalus with posterior dislocation of the body. Operative reduction followed. *B* and *C*, condition one year and nineteen days later. The fracture is ununited, and the entire astragalus is denser than the surrounding atrophied bones, indicating necrosis.

Fig. 6 (case 3).—*A*, photograph of cut and fractured surfaces; *B*, roentgenogram of slices, and *C*, microscopic sections of the two dead fragments excised fifteen months after injury. Fibrous invasion and partial creeping substitution are indicated by *x* in the lower half and upper margin of the head and neck, in the anterior margin along the fracture surface and in the posterior superior part of the body.

but the head laterally displaced and overriding the body, with apparent nonunion. The shadows cast by both the body and most of the head were denser than those of the adjacent bones, which showed evidence of atrophy of disuse. Because of persistent disability, the entire astragalus was excised by Dr. G. T. Aitken fifteen months after injury. Examination of the specimen showed that there were

lateral displacement and overriding of the head on the body, with fibrous union of the two. The body had been incompletely fractured during the operative removal.

Figure 6 shows a photograph, a roentgenogram and a stained microscopic section of slices excised sagittally from the two fragments. The lower half of the surface of the body is irregular, owing to a fracture produced during excision. The microscopic section shows the changes best. Both fragments apparently had become necrotic, although it is possible that some of the lower part of the head remained alive. The body fragment still consisted of necrotic bone and marrow except for narrow strips along the posterior superior margin and the whole of the anterior fracture margin, where there had been fibrous invasion and partial creeping substitution by living bone (x). The lower half and the superior margin of the head fragment had also been invaded and partly replaced (x). Figure 7 *A* is a section at the middle of the ankle joint surface of the astragalus, showing necrotic bone and marrow and poor staining of the deeper portion of the articular cartilage. The section in figure 7 *B*, from the anterosuperior portion of the body (x), illustrates the process of repair as it crosses the dead bone, the fibrous zone and the zone of creeping substitution.

One reason for the very slight invasion and creeping substitution of the body of the astragalus was the limited number of periosteal surfaces where adhesions could form and give opportunity for blood vessel and osteogenic tissue ingrowth. This could not occur over the extensive cartilage-covered surfaces. In contrast the head, with its greater periosteal surface, was proportionately more invaded and transformed.

The main artery to the astragalus is a branch of the dorsalis pedis artery, which gives branches to the bone along the lateral and inferior junctions of the neck and the body. It is prone to injury in cases of fracture of the neck. If in addition there is complete backward or rotation downward dislocation of the body of the astragalus, the likelihood of aseptic necrosis is greatly increased. This lesion should receive more attention, as it is a cause of nonunion and of poor functional results with fractures of the astragalus.

Fracture of the carpal navicular bone results in severance of the blood supply and necrosis of the proximal fragment in a relatively large percentage of cases. Rarely there is also devitalization of appreciable amounts of the distal fragment. Bony union of the fracture may take place in the presence of aseptic necrosis, but it greatly increases the frequency of nonunion. In the event of bony union, the bone of the dead fragment may be gradually absorbed and replaced by new bone. In some cases central replacement is incomplete, giving the roentgen appearance of cavitation. In other cases the necrotic fragment may

partly collapse. If nonunion results in the presence of necrosis, there are usually much functional disability and atrophy of disuse of the living bone, causing the more dense, nonatrophic necrotic fragment to

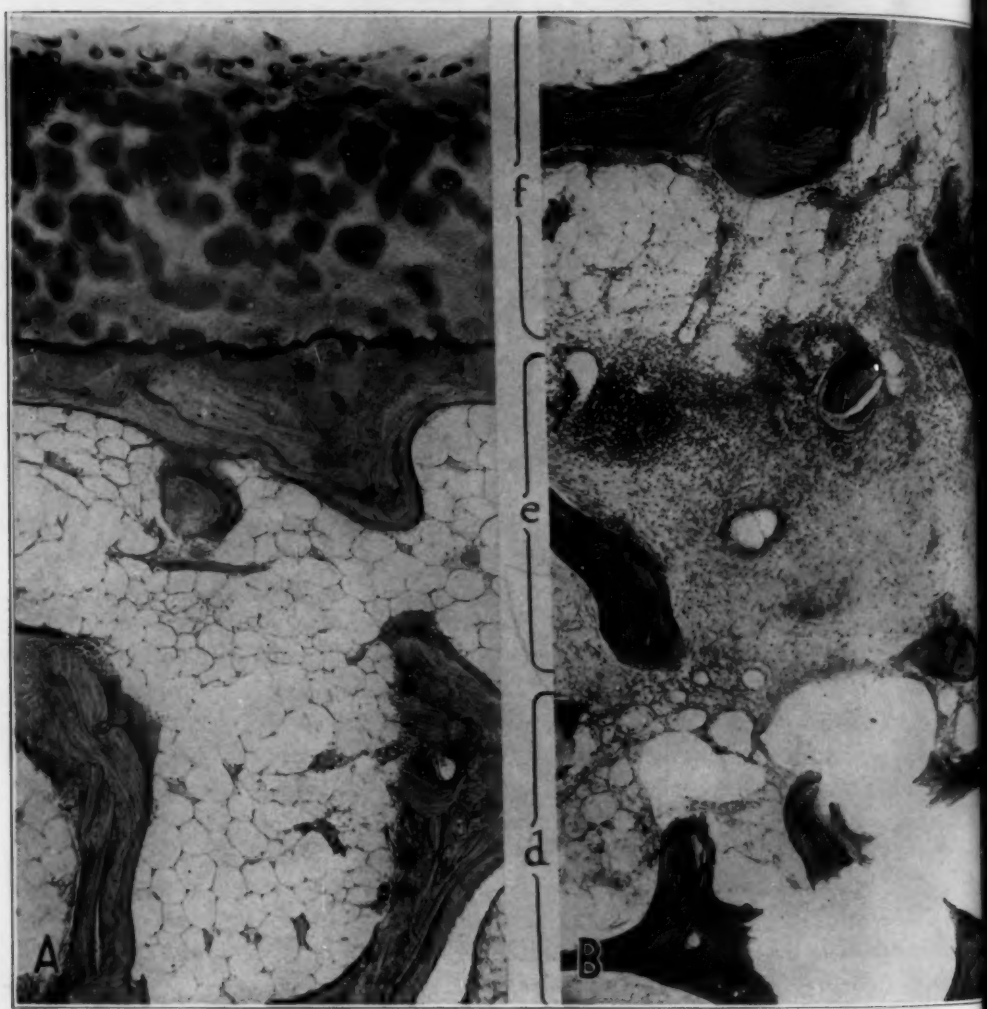

Fig. 7 (case 3).—*A*, middle of ankle joint surface of body. The bone and marrow are necrotic. The cartilage stains poorly, and the surface is eroded. *B*, section of the invading zone at *x* in figure 6, showing (*d*) old dead bone, (*e*) zone of fibrous invasion and (*f*) zone of replacement by new bone and marrow.

stand out in contrast in the rontgenograms. Also, vascular and fibrous invasion and creeping replacement take place at a slow rate, because articular cartilage covers by far the larger part of the surface of the

proximal fragment, which precludes invasion there. These pathologic and roentgen aspects are presented in the following reports.

CASE 4.—A man aged 29 sustained a fracture of the right carpal navicular bone, as shown by a roentgenogram taken the same day (fig. 8*A*). The treatment was by immobilization in a cast. In a roentgenogram taken ninety-three days later (fig. 8*B*) there was evidence of nonunion of the fracture and of reduced osseous density from atrophy, except in the proximal fragment (*x*), which retained its original density. The fragment was excised. There was fibrous union of the fracture, and the articular cartilage was grossly little changed except for damage produced in removal.

In a microscopic section (fig. 9*A*) the bone and marrow were seen to be necrotic and free from invasion except at one edge (*x*), where there were a small

Fig. 8 (case 4).—*A*, recent fracture of navicular bone. *B*, condition ninety-three days after injury. There was nonunion of the fracture; the necrotic proximal fragment (*x*) possesses greater density than the surrounding living bones, which show atrophy from disuse.

amount of fibrous ingrowth and partial replacement of dead bone by new bone (fig. 9*B*). Cartilage staining was somewhat reduced.

If the necrotic fragment is not removed it may undergo slow creeping substitution, or the interior may be absorbed but not replaced by bone, giving a honeycombed appearance in the roentgenograms. Adhesions, partial necrosis of cartilage, irregularity of articular surface and chronic arthritis are frequent late results, as is shown by the reports of Speed and others.[13]

13. Speed, K.: Fractures of the Carpus, J. Bone & Joint Surg. **17**:965, 1935; A Text-Book of Fractures and Dislocations, ed. 3, Philadelphia, Lea & Febiger, 1935.

Intra-articular fracture of a normal bone with complete separation of a fragment consisting of bone and articular cartilage is most frequently seen in cases of fracture of the head of the radius and of the lower articular surface of the humerus, but it may occur in other regions, such as the head of the femur, where a chip is detached. If the detached fragment is entirely displaced from its bed, it rarely remains a free body but becomes attached to the lining of the joint. In this useless position it

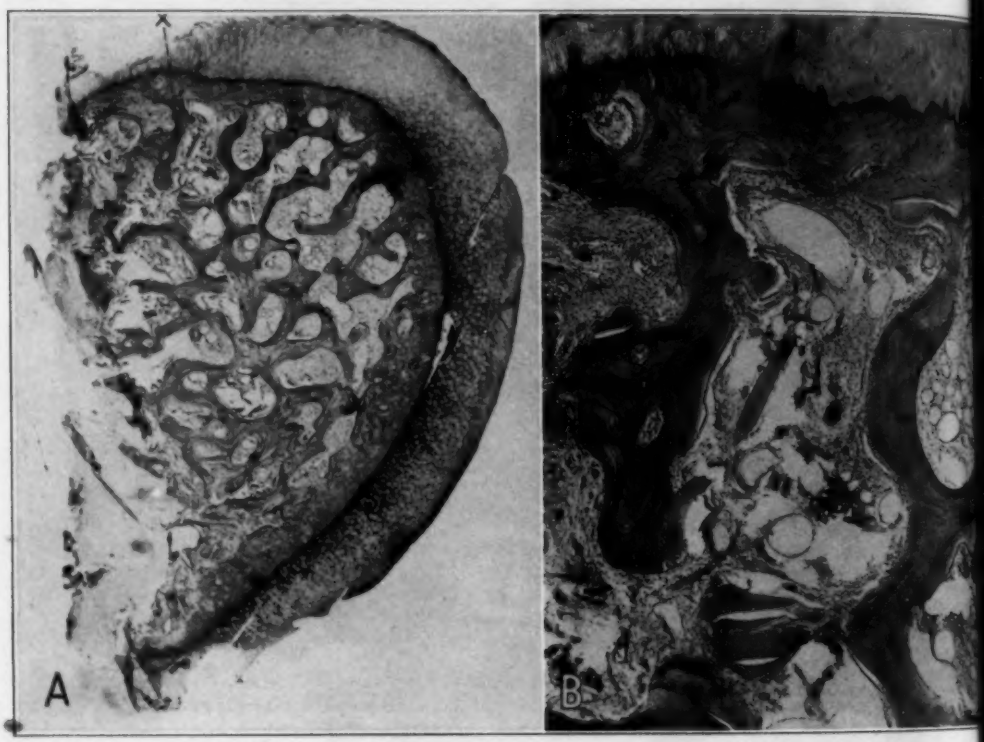

Fig. 9 (case 4).—Excised necrotic fragment of navicular bone. *A*, microscopic section; cartilage staining is slightly diminished. The bone and marrow are necrotic except at *x*, where beginning invasion and replacement may be noted. *B*, high power photomicrograph taken at *x*, showing connective tissue and blood vessel invasion and beginning replacement by new bone and marrow.

has no supporting function to perform; consequently, although it becomes revascularized and gradually replaced, the replacing tissue contains much less bone than when the fragment becomes united in a useful position. Eventually it may be largely absorbed. At the articular end of the humerus the capitellum, in some cases with a portion of the trochlea, is detached, rotated and displaced anteriorly and upward, where it becomes attached and imperfectly replaced by new bone, as in the following case.

CASE 5.—A man had been injured six months previously. Roentgenograms (fig. 10) revealed the anteriorly displaced and rotated condyles with both their cortical and their cancellous bone casting shadows greatly reduced in density. At operation the cartilaginous surface of the fragment was loosely adherent to the

Fig. 10 (case 5).—Six month old intra-articular fracture of the capitellum and part of the trochlea of the humerus with forward and upward displacement and bony attachment within joint. Note (*x*) the capitellum and (*y*) the trochlea.

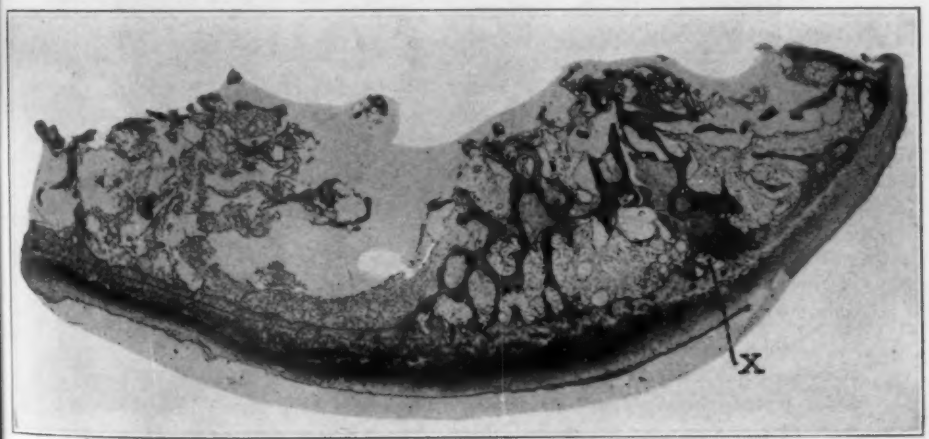

Fig. 11 (case 5).—Section of excised capitellum. The heavily trabeculated portion is old dead bone; the rest is delicate new replacement bone and marrow. The cartilage is intact, but staining is impaired in parts.

synovial lining, and its base was united by bone to the underlying cortex. It was excised and found to consist grossly of cartilage that was little changed and of bone that was extremely porous and filled mainly with fatty marrow. A microscopic section (fig. 11) showed only a small amount of the old heavy trabeculated bone left, which was necrotic and had fibrous invasion of its marrow spaces.

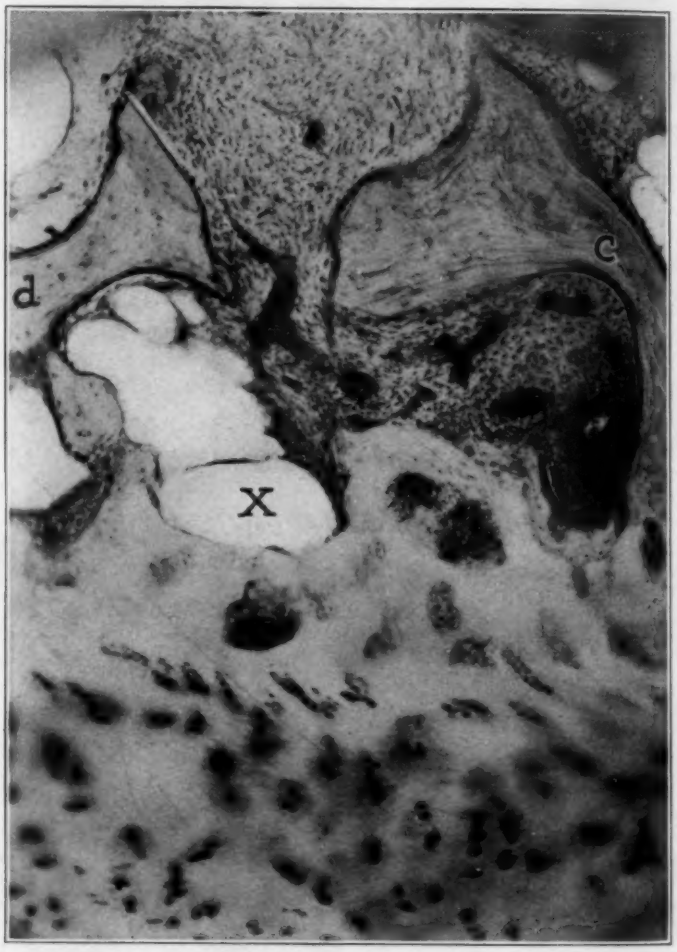

Fig. 12 (case 5).—Higher magnification at *x* of figure 11, showing the zone of creeping replacement of dead bone (*c*) by new bone (*d*). Most of the cartilage cells stain.

It extended to the cartilage only at *x*, and creeping substitution was in progress along its periphery. The rest of the cortex and trabeculated bone had been replaced by extremely delicate new bone. The marrow was composed of fat, a loose connective tissue framework and scattered hemopoietic cells. Figure 12 shows the region (*x*), with dead bone, and fibrous marrow being replaced by

new bone. The cartilage here and elsewhere, with regenerated blood vessels along its underlying surface, showed normal staining of the majority of nuclei. Had this fragment not been excised there would no doubt have been later absorption of cartilage and further removal of bone.

A similar fracture was seen in which only slight anterior rotation displacement resulted. There was bony union ten months later, with the condyles functioning and casting shadows of normal density. In the presence of activity they had apparently been replaced by a normal amount of bone.

Interruption of the blood supply with subsequent necrosis of the head of the femur produced by fractures of the intracapsular portion of the neck has already been so fully reported on [14] that it will not be reviewed in detail. It constitutes by far the most important lesion produced by interruption of the circulation in bone, because of its great frequency and because of its adverse effects, which are still all too little realized by the members of the medical profession. The blood supply of the head of the femur is derived from arteries which reach it principally by way of the capsule of the neck, especially posteriorly and by way of the round ligament. There appears to be a good deal of variation in the blood supply coming from each set of vessels and also in the extent of collateral circulation between the two. The indications are that in adults end arteries are more common in the head of the femur than in any other part of the skeleton, and necrosis from causes other than trauma is often located here.

In case of death of the head from injury to the vessels, the fracture may either unite or remain ununited. Union of the fracture is much more apt to occur if it is impacted or if there are accurate reduction and operative fixation. It occurs by formation of a fibrous callus in the cancellous spaces of the distal end of the neck, which grows across the fracture line and into the cancellous spaces of the proximal fragment. No periosteal or peripheral callus forms, and the fibrous callus is transformed directly into bone without the appearance of cartilage in the process, as was recently pointed out by Felsenreich.[15] Vascularized connective tissue then begins to invade the head and to break down and replace the dead marrow. The invasion may take place from the callus which bridges the fracture line, from portions of capsule which may remain untorn and from the round ligament. Metaplasia of the invading

14. (*a*) Santos, J. V.: Changes in the Head of the Femur After Complete Intracapsular Fracture of the Neck: Their Bearing on Non-Union and Treatment, Arch. Surg. **21**:470 (Sept.) 1930. (*b*) Phemister, D. B.: Fractures of Neck of Femur, Dislocations of Hip, and Obscure Vascular Disturbances Producing Aseptic Necrosis of Head of Femur, Surg., Gynec. & Obst. **59**:415, 1934; The Pathology of Ununited Fractures of the Neck of the Femur with Special Reference to the Head, J. Bone & Joint Surg. **21**:681, 1939.

15. Felsenreich: Histologische Untersuchungen an operierten Schenkelhalsbrüchen, Arch. f. klin. Chir. **192**:490, 1938.

connective tissue or fibrous callus into new bone and bone marrow is soon established and progresses into the head simultaneously with and a short distance back of the fibrous invasion. This creeping replacement occurs gradually, and the neck is transformed soon after the healing of the fracture. But the head is usually still mainly untransformed at the completion of bony union of the fracture, and the process may continue for months or years before it is either completed or comes to a standstill. The new bone which replaces the dead bone after union is complete and some function has returned to the limb is soon about as dense as the old bone, for which reason it is difficult to recognize creeping substitution following fracture with bony union in roentgenograms. In how many cases the condition may go on to unrecognized complete reorganization is not known.

When the condition is recognized it is usually because of collapse of the superior untransformed portion of the head from premature weight bearing or because of late chronic arthritis. Collapse of the head may begin at any time from a few months to two or three years after healing of the fracture. The broken-down portion may be invaded and replaced by new bone in the course of time. But if an ununited fracture line is established between the broken-down and the transformed portions, the replacement may be greatly retarded, as in the following case, in which the rare opportunity was presented of confirming the roentgen diagnosis by pathologic examination.

Case 6 (Dr. Carl Badgley).—A woman had an impacted fracture of the neck of the femur (fig. 13 *A*), which was treated by rest. Bony union resulted. After walking was resumed, pain, stiffness and weakness set in and gradually progressed until, four years and two months later, she was badly crippled. A roentgenogram taken then (fig. 13 *B*) showed a dense, wedge-shaped area (*x*) extensively separated from the surrounding bone. The rest of the head cast mottled shadows and had a hazy articular cortex as compared with the early picture (*A*), which indicated transformation. The upper portion of the head was excised.

A microscopic section through most of the excised portion (fig. 14) included the broken-off wedge, which was separated from the surrounding bone by an irregular band of fibrous tissue at the left and at the base and a pseudoarthrotic line at the right. Its left edge was separated from the rest by a pseudoarthrotic cleft and consisted of substituted new bone covered by a thin layer of fibrocartilage. The main part of the wedge was capped by old articular cartilage of normal thickness, with the cells staining poorly and the matrix partly calcified. Underlying it, from (*d* to *e*), were old dead bone and dead marrow, with a small amount of bone dust which had been ground into its cancellous spaces. To the left of *e* was old dead bone which had been invaded by fibrous marrow, and at the deepest portion there had been some replacement by new bone. Figure 15 is a high power photomicrograph taken at *d*, showing the dead bone and marrow in the portion (*a*) and fibrous marrow throughout the dead bone (*b*) which was spreading into and replacing the dead marrow at *a*. Replacement of the dead bone by new bone had not yet started at *b* but was present farther to the left. Figure 16 *e*

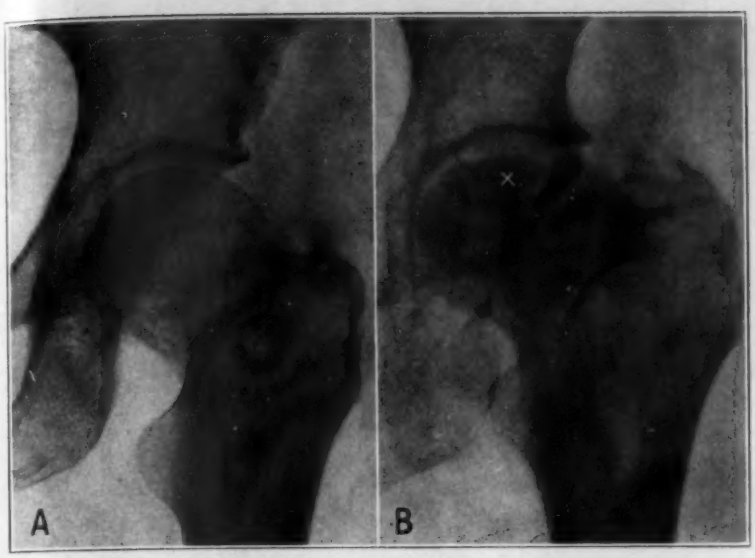

Fig. 13 (case 6).—*A*, recent impacted fracture of the neck of the femur. *B*, condition four years and two months later. The neck fracture is united. The head, which became necrotic, is flattened. The wedge-shaped remaining dead portion (*x*), with the original density and articular cortex preserved, is separated from the substituted portion, which is mottled and has a hazy shadow of new articular cortex.

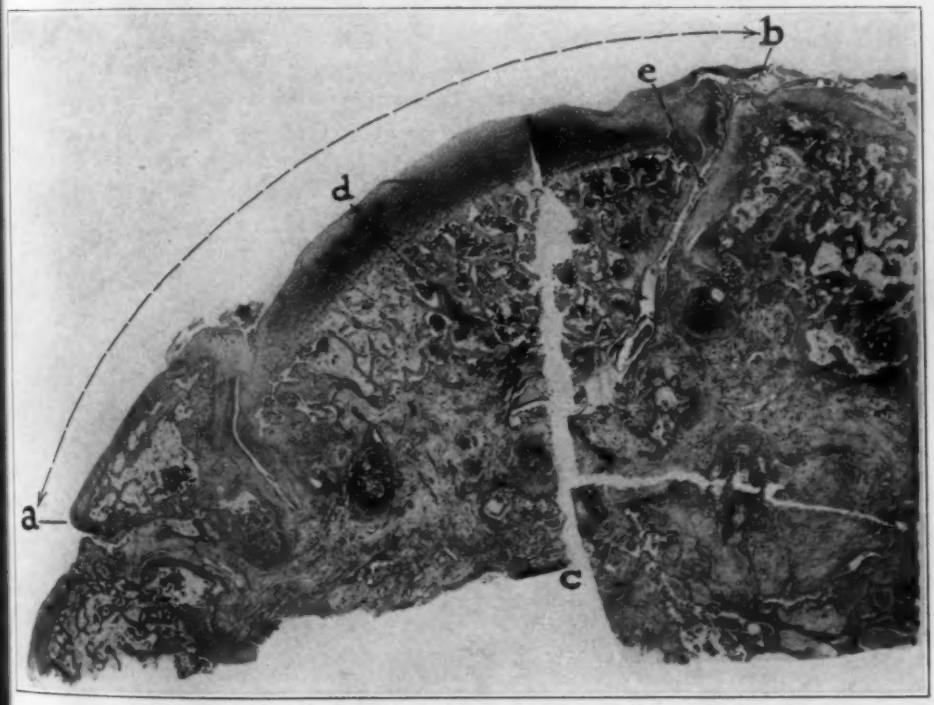

Fig. 14 (case 6).—Microscopic section of necrotic wedge (base *a-b* and apex *c*) extensively separated from the transformed portion by fibrous tissue like that of an ununited fracture line.

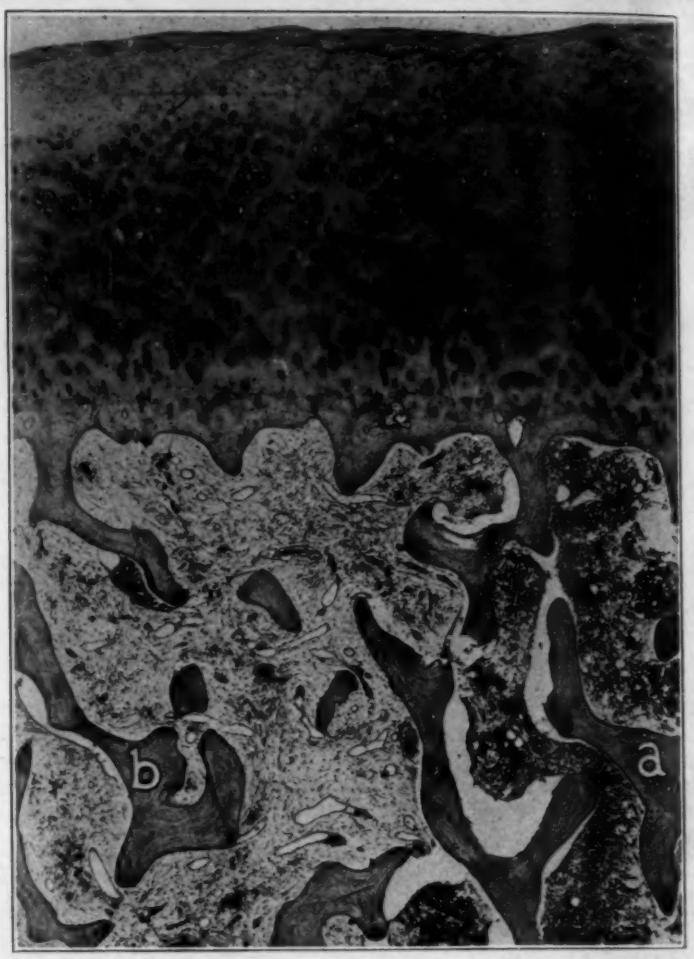

Fig. 15 (case 6).—High power photomicrograph of the necrotic wedge at *d* of figure 14, showing (*a*) dead bone and dead marrow uninvaded and (*b*) dead bone in which fibrous tissue has invaded and replaced the dead marrow.

Fig. 16 (case 6).—Pseudarthrotic fracture line at *e* in figure 14, separating the dead portion containing some bone dust in the marrow spaces (*a*) from the transformed living portion (*b*).

(through the pseudoarthrotic junction) shows necrotic bone and marrow infiltrated with some bone dust (*a*) and living bone (*b*) outside the necrotic area. The articular cartilage beyond the limits of the wedge consisted of a narrowed layer of fibrocartilage, and its underlying cortex was thin and uneven, showing that both had been transformed.

The following case is remarkable in its bearing on several aspects of devitalization of the head in fractures of the neck of the femur.

CASE 7.—A 96 year old woman sustained an impacted intracapsular fracture of the left hip (fig. 17 *A*). Treatment was by rest in bed, and the fracture united. She remained in bed for more than a year but after one and one-half years began to walk. Function gradually returned to normal, and she continued to be active until four years after the injury, when she again fell, fracturing the base of the neck of the right femur. Figure 17 *B* shows the roentgen appearance of

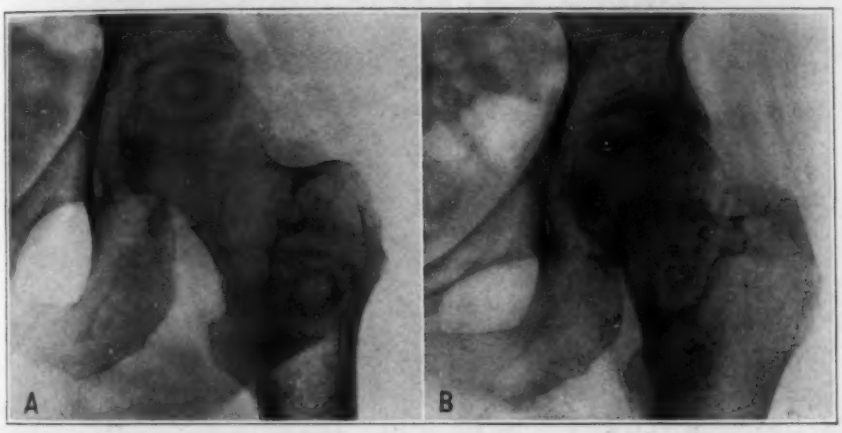

Fig. 17 (case 7).—*A*, fresh impacted fracture of the neck of the femur in a 96 year old woman. *B*, condition three and three-fourth years later. The fracture is united. The mottled trabeculae in the head suggest transformation.

the left hip three and three-fourths years after the fracture. The patient was bedridden after the fracture of the right hip until she died, four years later, at the age of 104 years, of carcinoma of the left breast.

At necropsy both hips were obtained. The right hip presented a normal picture aside from moderate coxa vara due to the healed fracture at the base of the neck (fig. 19 *A*). Microscopically the head was alive but atrophic, and the cartilage and synovia were intact except for senile changes. The left hip (fig. 18) showed bony union of the fracture. There was lipping at the margins of the articular cartilage of the head, most marked posteriorly (*A*). The cartilage was thinned and roughened in its weight-bearing portion but fairly well preserved mesially below the fovea and laterally beyond the line of contact with the acetabulum. The cartilage of the acetabulum was also somewhat roughened, thinned at its superolateral margin and fibrous in parts of its lower extent. There were one osteocartilaginous body free in the joint and two attached to the round ligament by narrow pedicles. There were two islands of ossification in the inferior portion of

the capsule and one in the round ligament. There were a few villous tags of the synovial lining. A slice 0.66 cm. thick was cut through the center of the femur and acetabulum. The cut surface of the head revealed in its inferomesial portion

Fig. 18 (case 7).—Necropsy specimens of the left hip eight years after fracture of the neck followed by bony union. *A*, posterior view; *B*, coronal section. Marginal lipping, osteocartilaginous loose bodies and cartilage erosion may be noted. The necrotic area is shown at *x*.

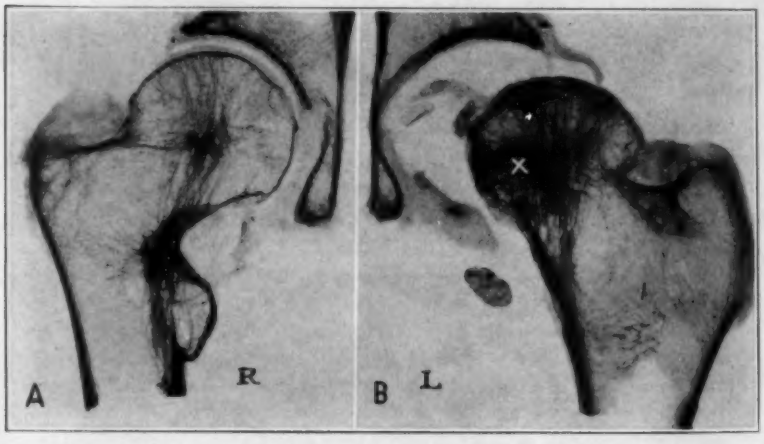

Fig. 19 (case 7).—Roentgenogram of slices of the hips. *A*, healed fracture of the right hip at the base of the neck; the head survived. *B*, healed intracapsular fracture of the neck (left hip). The head became necrotic and transformed except at *x*. Note the shadows of osteocartilaginous loose bodies.

a whitish, cricumscribed, necrotic-appearing area (fig. 18, *x*). A roentgenogram of the slice (fig. 19, *L*) shows the head in a slight valgus position as a result of the old lateral impaction. The light area (*x*) shows a narrow irregular ring

of increased density about it. The head cast dense shadows in the direction of the lines of stress and in the cortical and subcortical regions. There was increased density in the cortical and subcortical regions of the weight-bearing portion of the acetabulum. These changes were in marked contrast with those in the right hip (*R*). A microscopic section of the hip (fig. 20) revealed living bone throughout the head except at *x* and beneath the thick cartilage at the top of the head. In the latter region a small stretch of old cortex and of underlying heavy trabeculae were necrotic, and their cancellous spaces were filled with fibrous marrow. The lesion (*x*), which is seen magnified in figure 22 *A*, consisted of a central mass of necrotic bone and bone marrow which was immediately surrounded by a narrow calcified zone outside which was a thicker fibrous zone containing necrotic bony trabeculae. External to the fibrous zone were living bone and marrow, and along the surface were very slight indications of creeping substitution. This encapsulat-

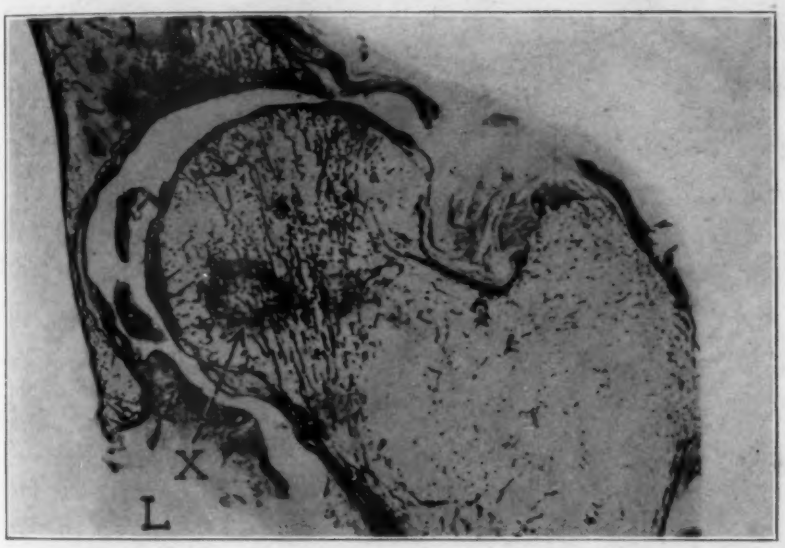

Fig. 20 (case 7).—Microscopic section of the left hip, showing mottled trabeculae and walled-off necrotic area (*x*) in the head and chronic arthritis and a loose body in the joint.

ing zone is shown in high power in figure 21 *A*. The necrotic area resembled the one (fig. 22 *B*) from a case of ununited fracture of the neck with death of the head of four and one-half years' standing. Here the zone of transformation was not calcified, but creeping substitution had almost come to a standstill in it. The articular cartilage of the head in the weight-bearing region was markedly thinned and frayed (fig. 21 *B*). Over the lateral portion of the head and beneath the fovea it was of normal thickness but stained poorly. Beneath the fovea the bone had penetrated into the cartilage from within and partly replaced it. The loose bodies attached to the ligamentum teres consisted of a mixture of hyaline and calcified cartilage and of cancellous bone. The free body contained only hyaline

and calcified cartilage. A microscopic section of the synovial lining showed slight villous formation and fibrous thickening.

In summary, an impacted fracture of the neck of the left femur in a 96 year old woman appears to have cut off the blood supply and resulted in necrosis of the head. Bony union followed, and in the

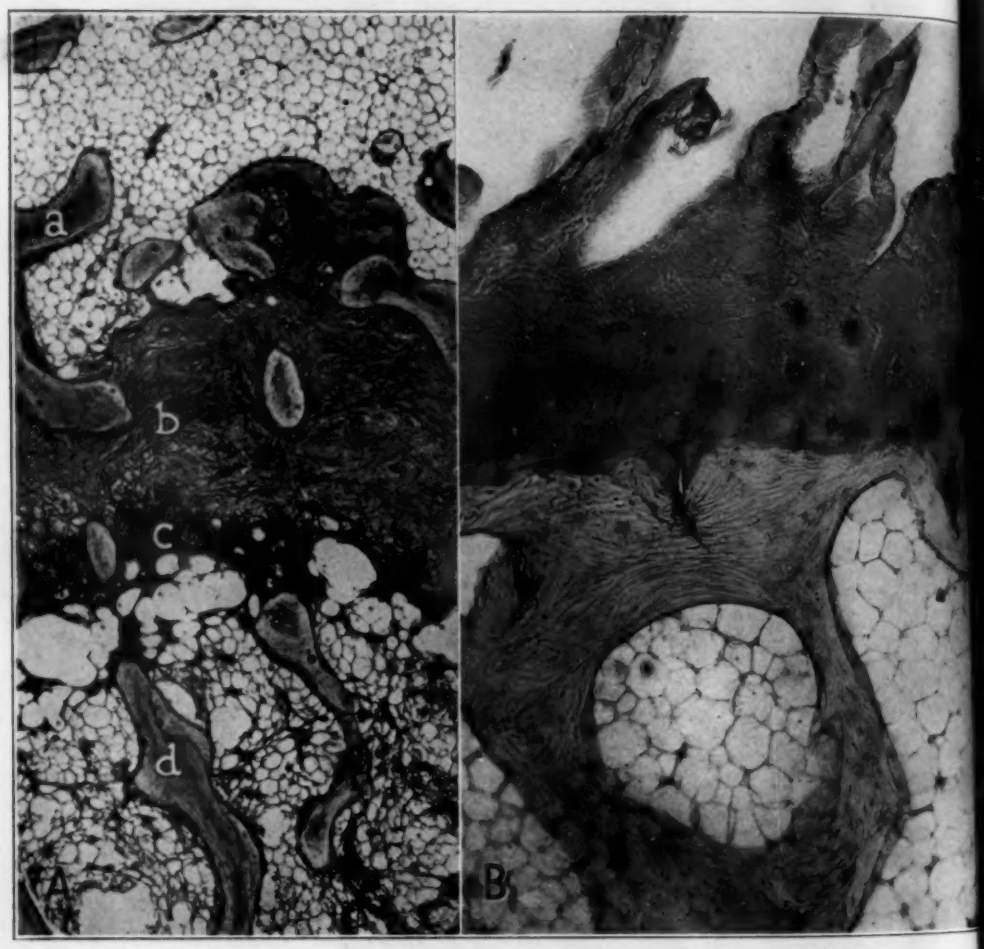

Fig. 21 (case 7).—*A*, periphery of the necrotic area in the head shown in figure 21 (*x*). Note (*a*) the surrounding living bone; (*b*) the fibrous zone; (*c*) the inner calcified zone, and (*d*) the central necrotic bone and marrow. *B*, weight-bearing surface of the head. The bone is alive; the cartilage is eroded and feebly staining.

absence of weight bearing for one and one-half years most of the head underwent replacement by living bone. Subsequent weight bearing did not cause collapse of the head. In the inferior and mesial portion replace-

ment came practically to a standstill, leaving, eight years after fracture, a necrotic island the fibrous capsule of which had calcified in its inner portion. There were necrosis and erosion of some of the articular cartilage and secondary formation of arthritis deformans and of osteo-cartilaginous loose bodies. The case offers proof of the fact that if weight bearing is avoided for many months after fracture there may be sufficient creeping replacement by new bone to prevent subsequent collapse of the

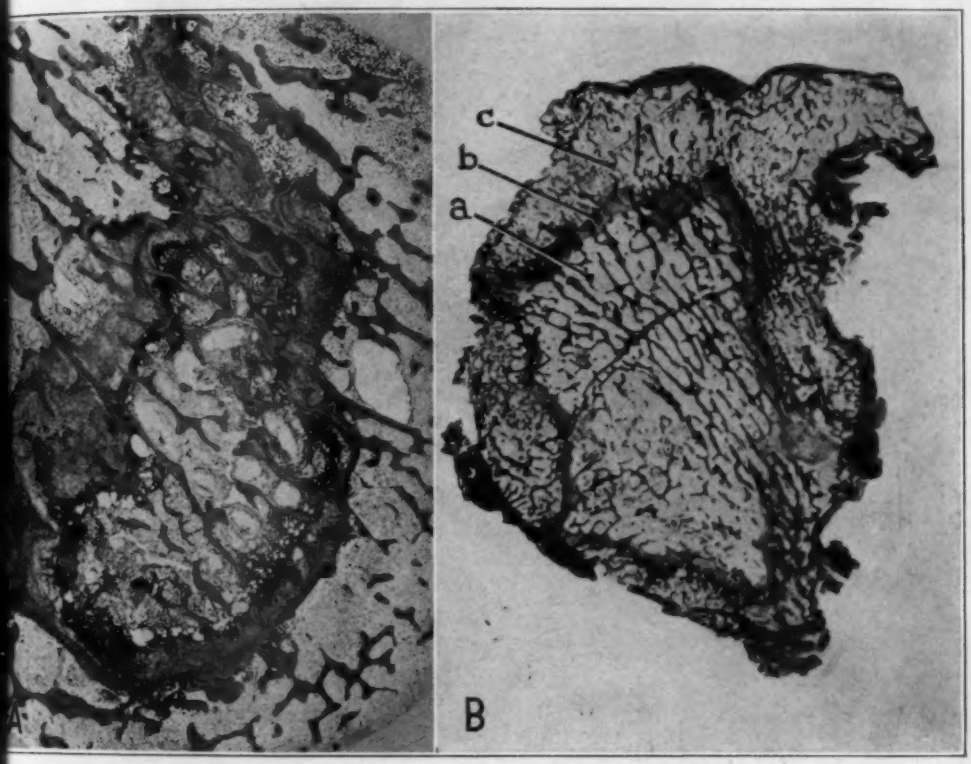

Fig. 22 (case 7).—*A*, another section of the walled-off necrotic area shown in figure 20. *B*, section of the head in the case of a four and one-half year old ununited fracture of the neck. There is a similar central necrotic area (*a*) surrounded by a fibrous zone of transformation (*b*) and then by substituted new bone (*c*). × 3.

head; it also shows that arthritis deformans may be a sequel of necrosis of the head without collapse of the weight-bearing portion.

Necrosis of the head associated with nonunion of the fracture of the neck has been studied at all stages, from a few days to many years after the injury. The changes may be summarized as follows. The entire bony head becomes necrotic in the great majority of cases, including the bone

and the bone marrow. Atrophy from disuse develops in the adjacent living bone, and in six to eight weeks the dead head is so much denser than the living bone that it casts a heavier shadow in roentgenograms. Revascularization and fibrous tissue infiltration of the marrow spaces begin within a few days to weeks by way of the round ligament, adhesions or any remaining untorn portion of the capsule. This usually

Fig. 23 (case 8).—Six month old ununited intracapsular fracture of the neck. The density of the head is normal in its upper portion and irregularly reduced mesially and inferiorly (*x*). This indicates a necrotic head with partial substitution by new bone.

progresses slowly and is followed by a zone of metaplasia in which there is absorption of the old dead bone and creeping replacement by a less dense new bone than is laid down when the fracture unites. A head in the process of replacement was studied in the following case.

CASE 8.—A 52 year old man fractured the left hip six months before admission. A roentgenogram (fig. 23) revealed nonunion with rotation of the head and

irregular reduction in density in its inferior and mesial portions as compared with the more uniform superior portion. "Disuse atrophy" of the lower fragment was seen. The head was excised, and a Whitman reconstruction operation was performed. There were whitish calcium deposits in large synovial villi, in the untorn portions of the capsule and in the round ligament. A roentgenogram and a microscopic section were made of a slice cut coronally from the head (fig. 24). The roentgenogram shows marked reduction in density lateral to the fovea, with extensions upward, laterally and irregularly downward. In the superior and inferolateral regions the shadows of trabeculae were of even density and appeared to be unchanged.

On comparison of the roentgenograms with the microscopic section (*b*) it is seen that there were a large area at the top and a small area at the bottom of old dead bone and marrow (*c*) bordered by a zone of fibrous invasion and creep-

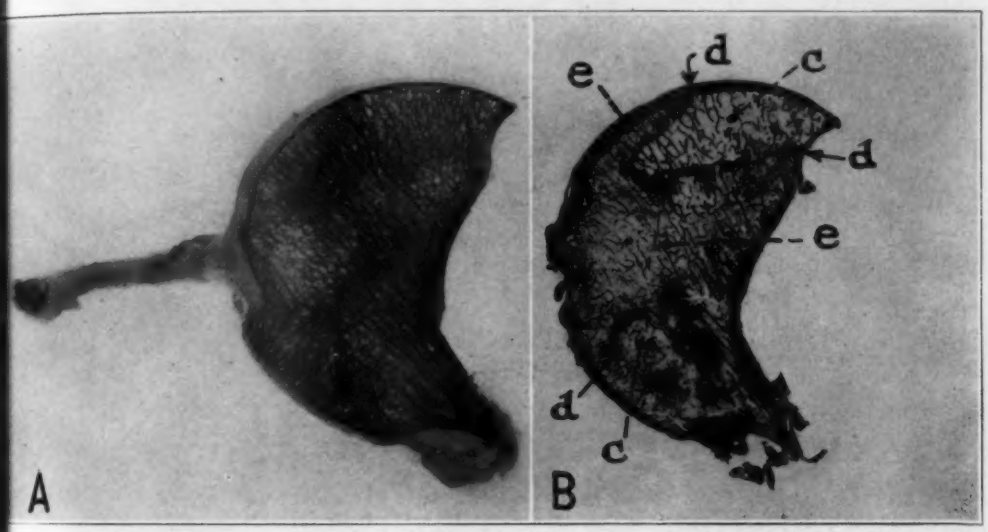

Fig. 24 (case 8).—*A*, roentgenogram of a slice of the excised head. The round ligament is partly calcified. There is mottled reduction in density in regions where dead bone is replaced by new bone, especially about the fovea. *B*, microscopic section of the head. Note (*c*) the uninvaded dead regions, (*d*) the zones of invasion and replacement and (*e*) the substituted living region.

ing substitution (*d*). The rest of the section (*e*) had undergone invasion and extensive creeping replacement by a more spongy living bone and living marrow, although along the middle and inferior portions of the eroded fracture surface there were old dead trabeculae, which accounted for the greater density. The cartilage was grossly intact, but microscopically its staining properties were reduced; however, the cartilage cells stained much better in the regions where the underlying bone had been revascularized and substituted than over the dead area at the superior portion. Figure 25 shows regions *c*, *d* and *e* in greater magnification.

Transformation was taking place rather rapidly in this head, and in the plane of the microscopic section only about one third of the old dead

bone and marrow remained uninvaded. Microscopic sections of the round ligament revealed several fair-sized blood vessels which probably had hypertrophied and were supplying blood to the head. A unique observation was the calcium deposits in the round ligament and in synovial villi in richly cellular areas of connective tissue.

That operation in a case of ununited fracture with necrosis of the head may result in a successful outcome with rapid replacement of the remaining dead bone is illustrated by the following case.

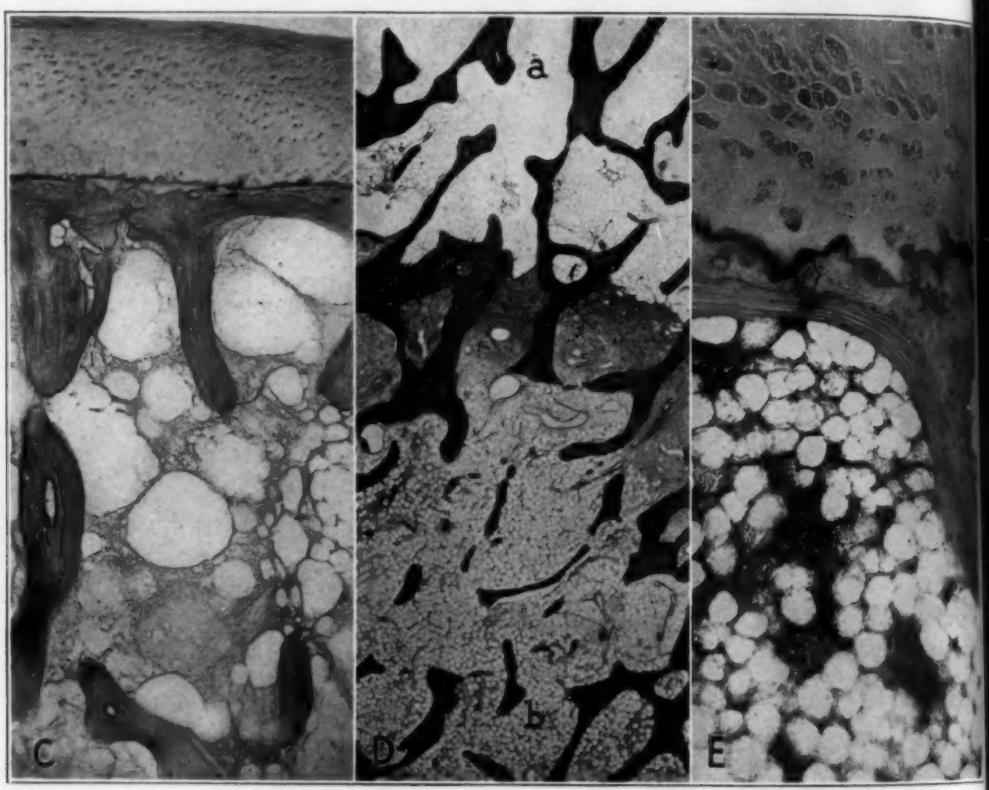

Fig. 25 (case 8).—High power of section *B* of figure 24. *C*, uninvaded upper portion; the bone and marrow are dead. The cartilage stains feebly. *D*, zone of invasion and replacement. Note the dead bone (*a*) and the substituted new bone (*b*). *E*, a cortical field of the replaced region. The bone is alive, and the cartilage stains fairly well, with its nutrition improved by the reestablished underlying circulation.

Case 9.—A woman aged 52 had an ununited fracture of ten months' duration. A roentgenogram (fig. 26*A*) showed areas of markedly reduced density in the lower portion of the head and an even shadow of about the normal density in

the upper portion of the head. Between the two and bordering on the eroded surface was an irregular zone of increased density. The findings indicated that there was death without invasion and replacement of the upper part of the head, creeping substitution of the lower part and possibly eroded bone meal infiltration of the marrow spaces between, accounting for the increased density. The fracture was operated on by insertion of two bone grafts and three threaded wires for fixation, after the method of Compere.[16] Figure 26 *B* shows the appearance after two months and figure 26 *C* the appearance after thirteen and one-half months, the wires having been removed five months previously. The fracture had united, and the upper necrotic portion of the head, which had been extensively bored and replaced by the transplants, appeared to have been replaced by living bone, with preservation of the normal contour. The patient used crutches for ten months, after which there was weight bearing, with excellent results.

Long-standing ununited fracture of the neck of the femur with necrosis of the head is also not infrequently complicated by cartilage

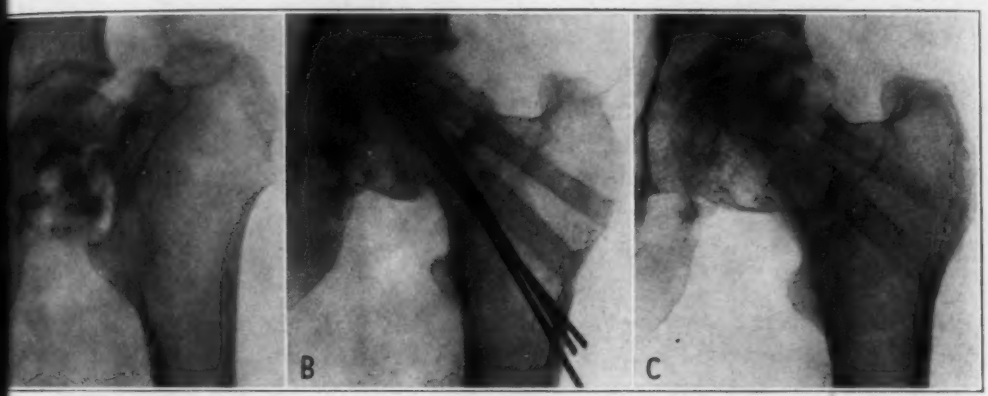

Fig. 26 (case 9).—*A*, ununited fracture ten months old, with death of the head and about one half of it substituted for by less dense new bone. The upper portion is dense old dead bone. The lower portion is spongy new bone. *B*, condition thirty days after fixation by three threaded wires and two bone grafts. *C*, condition thirteen and one-half months after operation and five months after removal of the wires. The fracture is united and the head largely transformed.

adhesions, osteocartilaginous loose bodies and mild synovial changes of arthritis deformans. If there is complete absorption of the necrotic area, the interior of the head may contain few trabeculae and give the roentgen appearance of a cavity. If the replacement comes to a standstill, the necrotic area located centrally or in the superior portion may continue to cast a dense shadow for years, as in the case illustrated by figure 22 *B*.

16. Compere, E. L.: The Restoration of Physiological and Anatomical Function in Old Ununited Intracapsular Fractures of the Neck of the Femur, J. Bone & Joint Surg. **22**:261, 1940.

DISLOCATIONS

Poor functional results following traumatic dislocations of the hip were reported by the older surgeons and attributed to chronic arthritis. It was not until after Axhausen described fracture of the neck of the femur followed by necrosis of the head, bony union and subsequent collapse of the head that the bad results following dislocation of the hip were recognized as due to necrosis of the head. Mueller reported the first case in 1924,[4] and since then the condition has been recognized with increasing frequency. In the cases in which diagnosis has been made the changes have been similar to those associated with fracture of the neck with necrosis of the head, bony union and subsequent breaking down of the head. After reduction of the dislocation there is sometimes a period of several months to a year of relative freedom from symptoms and a normal roentgen picture. Then weakness, stiffness and pain set in and gradually progress, and roentgenograms reveal the changes. Banks [17] has recently reviewed 11 cases studied in this department or in consultation and has collected 39 cases reported in the literature. Among the patients were 8 children, in all of whom there was transformation of the head, with good results. In practically all of the 42 cases of fracture in adults the joint remained markedly deformed, and the functional results were poor. The cause of the necrosis has not been definitely determined. The round ligament was torn in all cases, whether or not there was an associated fracture of the acetabulum. When it constitutes an important source of blood supply to the head, the necrosis may result from its tear. It is possible, however, that the anterior or posterior circumflex arteries to the neck are also injured in the dislocation. The following case illustrates the changes.

CASE 12.—A man aged 61, seen in consultation with Dr. W. B. Carroll, had dislocated the right hip twenty-six years previously. The dislocation had been reduced, and there had been complete restoration of function, which had persisted. Recent roentgenograms had shown a normal appearance of the right hip. Eighteen months previously the patient had suffered a dislocation of the left hip with fracture of the posterior acetabular margin (fig. 27 *A*). Eighty-one days after reduction the head of the femur appeared normal in roentgenograms. Weight bearing was then resumed, but the hip gradually became more painful and restricted in motion. A roentgenogram taken nine months after the injury revealed beginning deformity of the head. Despite the use of a walking caliper

17. Banks, S.: Aseptic Necrosis of Femoral Head Following Traumatic Dislocation of the Hip, J. Bone & Joint Surg., to be published.

splint, this increased and figure 27 *C* shows the result eighteen months after injury. Necrosis of the head is doubtless the usual explanation of "chronic arthritis" following dislocation of the hip.

About the only other dislocation to result in interruption of the blood supply of the bone without associated fracture is that of the carpal lunatum. When this bone is completely dislocated anteriorly all of its dorsal attachments are torn, and, since the blood supply comes mainly through them, its circulation is usually interrupted, and the bone becomes necrotic. The displaced bone is in a more or less useless position, and if it remains there for a long time it eventually undergoes creeping substitution by bone of greatly reduced density similar to that of the

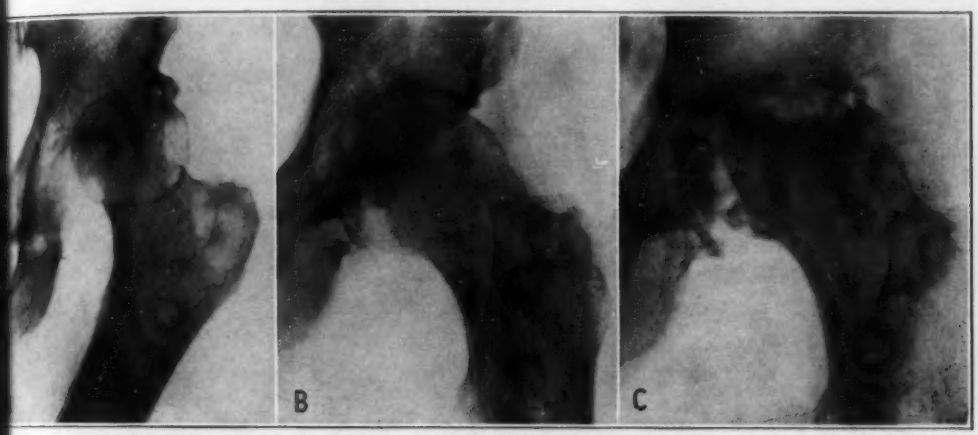

Fig. 27 (case 10).—*A*, recent dislocation of the hip, with a chip off the posterior acetabular margin. *B*, condition eighty-one days after reduction. *C*, condition eighteen months later.

broken-off and displaced condyles of the lower end of the humerus in case 5 (fig. 11).

A not uncommon injury is that of fracture of the navicular bone, with perilunar carpal luxation in which the lunatum and the proximal fragment of the navicular bone are subluxated anteriorly, while the remaining bones of the carpus are subluxated posteriorly. The blood supply of both the proximal navicular fragment and the lunatum may be interrupted, with resultant necrosis. This is illustrated in the following case.

CASE 11.—A man 29 years old injured his wrist thirty-eight days before examination. Figure 28 *A* reveals the roentgen appearance at that time. The hand had been in a splint, and the bones surrounding the anteriorly subluxated

lunatum and the proximal fragment of the navicular bone were atrophic and cast slightly fainter shadows than the latter. The dislocation was then reduced by open operation, and the wrist was immobilized for eight weeks. A roentgenogram taken ninety-six days after injury (fig. 28 *B*) showed that the lunatum and the adjacent navicular fragment had retained their original density, while the surrounding bones were still more markedly atrophic and reduced in density and the fracture was ununited. Excision of the necrotic bones was advised, but the patient refused operation.

Late changes similar to those associated with Kienböck's disease should be anticipated in cases of reduced dislocation of the lunatum.

Arthroplasty of the hip joint has not infrequently resulted in good restoration of free motion, but after weight bearing is resumed the joint slowly breaks down, with erosion of much of the remaining portion of the head and sometimes of part of the neck of the femur. The end result is a poorly functioning and frequently painful hip with varying degrees

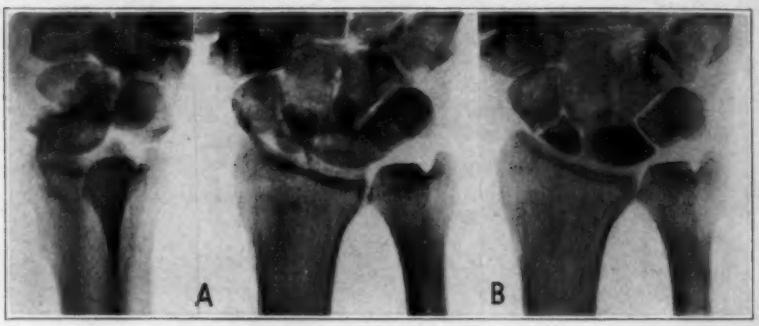

Fig. 28 (case 11).—Necrosis of the dislocated lunatum and proximal fragment of the navicular bone. *A*, thirty-eight days after injury. Note the slightly reduced density of the other bones from atrophy. *B*, ninety-six days after injury. Note the markedly reduced density of the other bones from atrophy, causing the unatrophied lunatum and navicular fragment to stand out.

of restriction of motion. In some cases, as that reported by me,[14b] the roentgen evidences of necrosis of the remaining portion of the head are very striking, and the subsequent reduction in size and invasion and replacement of the dense necrotic bone by new bone can be followed in roentgenograms. The reason for necrosis is that conditions similar to that of dislocation of the hip are created by the operation. In fact, the likelihood that capital necrosis will follow arthroplasty should be greater than the likelihood that it will follow dislocation, since the practice advocated by Murphy of excising the capsule of the neck which contains blood vessels going to the head, has been extensively followed. Instead of excising the capsule of the neck, every effort should be made not to

disturb it and to preserve the blood supply of the detached and refashioned head. In the following case of arthroplasty the indications are that the head disappeared rapidly as a result of erosion following aseptic necrosis.

CASE 12.—A woman aged 34 had bony ankylosis of the right hip following infectious arthritis two years previously, which had healed without drainage. During arthroplasty the capsule of the neck was excised, and the head was capped by free fascia lata. The wound healed by primary union and figure 29 shows the roentgen appearances twenty-two days, nine and one-half months and two and one-third years respectively after operation. As the head was eroded, the weakness and disability in the joint increased, and, although motion was free, the patient resorted to the use of a crutch two years after operation. Too little attention has been paid to aseptic necrosis as a cause of bad results following arthoplasty.

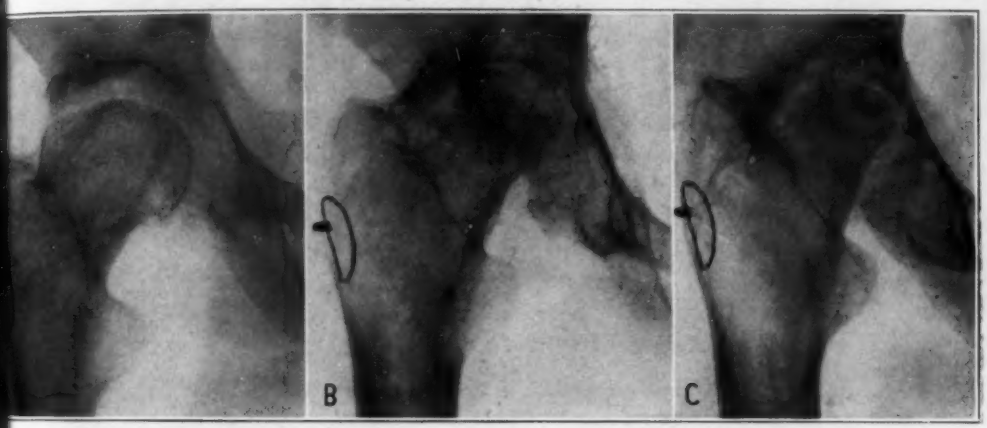

Fig. 29 (case 12).—Necrosis and erosion of the head of the femur following arthroplasty. *A*, twenty-two days after operation; *B*, nine and one-half months after operation; the uneroded portion of the head is slightly denser than the atrophied trochanter and neck; *C*, two and one-third years after operation.

SUMMARY AND CONCLUSIONS

The general pathologic and roentgen aspects of necrotic bone resulting from simple interruption of circulation and its repair are reviewed, and cases in which the lesion was produced by the trauma of fracture, dislocation and operation are specially considered.

In the presence of fracture of the shaft there is more or less devitalization from injury of the circulation along the fragment ends. The necrotic bone undergoes creeping replacement by new bone and does not interfere with union of the fracture. In case of massive splinter formation or of extensive operative denudation of fragments there may be extensive necrosis of bone, which later undergoes creeping replacement similar to

the changes in a transplant. In some cases it may be a factor in the causation of nonunion.

Fractures bordering on joints in certain locations may result in extensive to complete severance of connections and necrosis of the bone of the articular fragment. This is oftenest seen in fractures of the neck of the femur, the carpal navicular bone and the condyles of the humerus. There is predisposition to nonunion by displacement and by interference with callus formation from the articular fragment.

The articular cartilage undergoes more or less nutritional disturbance, which contributes to the later development of arthritis deformans and osteocartilaginous loose bodies.

If the fracture does not unite, the dead bone is gradually invaded by blood vessels and fibrous tissue and is partially to completely absorbed and replaced by much less dense new bone.

If the fracture unites and the dead bone is protected from stress and strain, e. g., from weight bearing in case of fracture of the neck of the femur, it may be gradually replaced by new bone, and a fairly satisfactory functioning joint may be obtained. If there is too great stress and strain, the bone collapses, and the joint becomes deformed. In case of failure of complete substitution in the head of the femur, the remaining necrotic bone may become surrounded by a calcified fibrous capsule.

Dislocation of the hip may result in interruption of the blood supply and necrosis of the head of the femur. There may be subsequent collapse from weight bearing or creeping replacement by new bone, as in the case of united fractures of the neck of the femur.

The pathologic picture in a case of fracture-dislocation of the astragalus is reported, in which there were necrosis of both fragments and nonunion of the fracture.

BUCCAL NEURALGIA

A FORM OF ATYPICAL FACIAL NEURALGIA OF SYMPATHETIC ORIGIN

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My reason for reporting on "buccal neuralgia" is that I have segregated a group of cases of a condition that falls into the general classification of atypical facial neuralgia but in which pain was limited to the cheek, upper jaw, malar region and nose. Moreover, a simple surgical procedure has been found that gave relief in a majority of these cases.

So-called atypical facial neuralgia is believed to originate in the sympathetic nervous system. Occasionally it is associated with "trigeminal tic douloureux," but it is not relieved by section of the sensory root of the fifth nerve. Atypical facial neuralgia is described as a deep-seated, dully aching, burning, throbbing, boring pain in the nasal, maxillary, zygomatic and temporal regions, in the jaw, in or behind the eye, in the nostril, in the cheek, in the gum and at times behind the ear, extending to the occipital region and occasionally down the neck. The pain is not lancinating but tends to be constant, lasting for several minutes to hours or even days. It varies in intensity, and exacerbations of intense sharp pain may occur.

Sluder's, or sphenopalatine, neuralgia is described as pain in the root of the nose and in and about the eye, extending from the upper jaw to beneath the zygoma and back of the ear and frequently to the neck and shoulder. Some patients have been relieved by cocainization or by injections into the sphenopalatine ganglion.

Vidian neuralgia is characterized by pain in the nose, face, eye, ear, head, neck and shoulder, occurring in severe attacks and relieved, as sphenopalatine neuralgia has been, by treating disease in the sphenoid sinus.

It will be noted that sphenopalatine and vidian neuralgia are similar to and belong in the group of atypical facial neuralgias.

These atypical facial neuralgias are differentiated from the ticlike pains referable to the fifth and ninth nerves, which are stabbing, lancinating, knifelike and momentary and which are readily induced by touch-

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ing or moving the areas in the anatomic distribution of the trigeminal or the glossopharyngeal nerves.

Sphenopalatine neuralgia was studied by Sluder [1] from 1908 to 1918 and remained as the chief neuralgia of the face other than true "trigeminal neuralgia" until Frazier and Russell,[2] in 1924, gave it the name of atypical facial neuralgia. They found over 100 cases of a condition that was not true "trigeminal neuralgia" and that failed to respond satisfactorily to any treatment.

Harris [3] in 1926 published his book on neuritis and neuralgia, which contained case histories of atypical facial neuralgia.

Fay [4] in 1927 called attention to the presence of tenderness to pressure over the carotid artery in the neck in cases of atypical facial neuralgia.

Frazier [5] in 1928 again discussed the unsuccessful treatment of atypical facial neuralgia by section of the various branches of the superior cervical sympathetic ganglion. Glaser [6] analyzed these cases of Frazier's, showing the similarity of symptoms, the lack of response to any treatment and the absence of any known cause. He divided them into ten groups, dependent on the location, extent and progression of the pain.

Peet [7] in 1929 expressed the belief that the pain of some of these atypical facial neuralgias originates in the sympathetic nervous system if due to vasomotor spasm, involving the sympathetic fibers on the external and internal carotid arteries.

It remained for Flothow [8] in 1930 and Mixter and White [9] in 1931 to report successful treatment of individual patients suffering from

1. Sluder, G.: Headaches and Eye Disorders of Nasal Origin, St. Louis, C. V. Mosby Company, 1918.

2. Frazier, C. H., and Russell, E. C.: Neuralgia of the Face: An Analysis of Seven Hundred and Fifty-Four Cases with Relation to Pain and Other Sensory Phenomena Before and After Operation, Arch. Neurol. & Psychiat. **11**:557 (May) 1924.

3. Harris, W.: Neuritis and Neuralgia, London, Oxford University Press, 1926.

4. Fay, T.: Atypical Neuralgia, Arch. Neurol. & Psychiat. **18**:309 (Aug.) 1927.

5. Frazier, C. H.: Atypical Neuralgia: Unsuccessful Attempts to Relieve Patients by Operations on the Cervical Sympathetic System, Arch. Neurol. & Psychiat. **19**:650 (April) 1928.

6. Glaser, M. A.: Atypical Neuralgia, So-Called: A Critical Analysis of One Hundred and Forty-Three Cases, Arch. Neurol. & Psychiat. **20**:537 (Sept.) 1928.

7. Peet, M. M.: The Rôle of the Sympathetic in the Atypical Neuralgias of the Face, Arch. Neurol. & Psychiat. **22**:313 (Aug.) 1929.

8. Flothow, P.: Relief of Pain from a Neurolgic Viewpoint, Northwest Med. **29**:69 (Feb.) 1930.

9. Mixter, W. J., and White, J. C.: Pain Pathways in the Sympathetic Nervous System: Clinical Evidence, Arch. Neurol. & Psychiat. **25**:986 (May) 1931.

atypical facial neuralgia by interruption of the cervicothoracic sympathetic ganglions after section of the sensory root of the fifth nerve had given no relief.

Migraine with associated phenomena referable to the sympathetic nervous system was successfully treated by Dandy [10] in 1931 and by Craig [11] in 1935 by "cervicothoracic sympathectomy."

Wilson [12] in 1932 believed that atypical neuralgia in some cases is psychogenic and advocated psychotherapy as the first treatment.

Two interesting papers on the mechanism of the atypical facial neuralgias were published in 1932. Fay [13] expressed the opinion that the distribution of pain in cases of atypical facial neuralgia follows the arterial vascular tree of the neck and head. His observations were made on patients with the region under local anesthesia. Stimulation by faradic current of the bifurcation of the carotid artery was extremely painful to the patient. The sheath of the vagus nerve, composed of fine fibers arising from the carotid artery, was also extremely sensitive. By appropriate stimulation of points about the bifurcation pain may be referred into the tongue, into the jaws, into the face, about the orbit, into the temporal or the occipital area, deep into the eyes and head and into the throat. His case 9 showed that stimulation at the bifurcation caused pain to be referred into the malar region and the face, especially when the facial artery as well as the external carotid artery was tested. Stimulation of the internal carotid artery produced pain deep in the parietal area. The various combinations of nerve sections performed by Fay led to the distinct impression that the vascular "pain fibers" of the head and face enter the cranial nerves, particularly the vagus near the bifurcation of the carotid. A considerable portion of the fibers pass down along the vascular structures of the neck to enter the lower cervical and upper thoracic portions of the cord. By producing limited spinal anesthesia at the first thoracic segment of the cord Fay found that the atypical neuralgic pain to the malar region and tenderness to pressure on the carotid artery disappeared. "The deductions obtained from these tests indicate that the pain fibers from the face follow the carotid arteries, the internal and external jugular veins and other vascular

10. Dandy, W. E.: Treatment of Hemicrania (Migraine) by Removal of the Inferior Cervical and First Thoracic Sympathetic Ganglion, Bull. Johns Hopkins Hosp. **48**:357 (June) 1931.

11. Craig, W. M.: Hemicrania of Migraine, Proc. Staff Meet., Mayo Clin. **10**: 362 (June 5) 1935.

12. Wilson, D. C.: Atypical Facial Neuralgia, J. A. M. A. **99**:813 (Sept. 3) 1932.

13. Fay, T.: Atypical Facial Neuralgia: A Syndrome of Vascular Pain, Ann. Otol., Rhin. & Laryng. **41**:1030 (Dec.) 1932.

structures and make their entry into the spinal cord in the upper three thoracic roots."

Davis and Pollock [14] in the same year presented evidence opposing the view of several observers that pain can be conducted antidromically over the anterior roots. These observers found that section of the posterior spinal roots and the fifth cranial nerve failed to produce complete analgesia, which then could be effected by sectioning the sympathetic chain. Davis and Pollock stated: "On an anatomic basis the sympathetic supply to the structures of the face and head must be considered as consisting of purely efferent fibers." Using cats, they found that stimulation of the superior cervical sympathetic ganglion produced pain whether the trunk was intact or severed below the ganglion. Stimulation of the ganglion after section of the anterior or posterior spinal roots produced pain. Stimulation of the ganglion after section of the anterior spinal roots and the posterior root of the trigeminal nerve produced pain. But stimulation of the ganglion after section of the posterior spinal roots and the posterior root of the trigeminal nerve caused no pain. On an anatomic basis, the fibers from the superior cervical ganglion join the trigeminal nerve by way of the carotid plexus and are distributed through it to the structures of the head and face. To explain the failure to secure relief from the atypical facial neuralgia by cutting the trigeminal nerve root and the superior cervical ganglion, Davis and Pollock offered evidence previously obtained that sensibility to pain on deep pressure is transmitted by the seventh cranial nerve. Their explanation of their experiments was that stimulation of the superior cervical ganglion produces an effect that is carried by way of postganglionic efferent fibers to structures innervated by the sympathetic fibers. These efferent impulses produce an effect on the skin and other structures, so that possibly a metabolite is liberated which in turn stimulates the ordinary sensory endings of the trigeminal nerve. This impulse is transmitted centrally and recognized as pain.

In their paper of 1936, Davis and Pollock [15] again proposed to show that it is only the efferent fibers of the autonomic system itself which are concerned with the production of pain and that such afferent fibers as travel along with it belong to the ordinary spinal sensory system. In cases of pain in the face, the only proved contribution of the autonomic system to the production of the pain is in relation to referred pain, in which the efferent, not the afferent, fibers are utilized.

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14. Davis, L., and Pollock, L. J.: The Rôle of the Sympathetic Nervous System in the Production of Pain in the Head, Arch. Neurol. & Psychiat. **27**:282 (Feb.) 1932.

15. Davis, L., and Pollock, L. J.: The Rôle of the Autonomic Nervous System in the Production of Pain, J. A. M. A. **106**:350 (Feb. 1) 1936.

Shaw,[16] in 1933, from clinical and experimental evidence, concluded that the sympathetic system possesses a sensory function and is concerned in the production of certain types of intractable neuralgia, since the residual sensation after division of the somatic innervation to an area of the body is dependent on fibers that traverse the ventral spinal roots, and these fibers are probably of sympathetic origin and pass through the anatomic sympathetic channels. This sensory residue is capable, Shaw found, of excitation by chemical stimuli of known sympathetic proclivity.

In 1934 I reported 5 cases of a combination of tic douloureux referable to the trifacial nerve and atypical facial neuralgia.[17] All the tic pains were relieved by interruption of appropriate branches of the trigeminal nerve, and 3 patients were relieved of the atypical neuralgia by alcoholic interruption of the cervicothoracic portion of the sympathetic chain.

Brickner and Riley [18] used the term autonomic faciocephalalgia for atypical migraine and atypical facial neuralgia and reported 3 cases of atypical migraine relieved by epinephrine.

Harris [19] reported again in 1936 on ciliary or migrainous neuralgia in which the pain is especially located in, behind or around the eyeball. In his classification of fifteen varieties of unilateral pain in the head and face he divided the atypical facial neuralgias into four groups, which he called: 1. Migrainous neuralgia, an anterior migraine probably due to a vasomotor neurosis of the meningeal vessels, which may be cured by block of the gasserian ganglion or nerve block. 2. Sympathetic hemicrania, with pain spreading to the back of the head and neck and associated with phenomena referable to the sympathetic nervous system. This may be relieved by intranasal spray of cocaine or by stellate ganglionectomy. 3. Chronic persistent neuralgia of the jaws, the temple and the side of the head and neck (Sluder's, sphenopalatine or vidian neuralgia), the algies sympathiques of the French writers, for which there is no treatment. 4. Facial psychalgia, clearly the result of a definite psychogenic factor and curable by psychotherapy.

In 1936 I described a form of atypical facial neuralgia about the teeth and cheek that was relieved by section of the facial artery, the vein

16. Shaw, R. C.: Sympathetic System and Pain Phenomena, Arch. Surg. **27**: 1072 (Dec.) 1933.

17. Reichert, F. L.: The Neuralgias of the Head and Face, Am. J. M. Sc. **187**: 362 (March) 1934.

18. Brickner, R. M., and Riley, H. A.: Autonomic Facio-Cephalalgia, Bull. Neurol. Inst. New York **4**:422 (Dec.) 1935.

19. Harris, W.: Ciliary (Migrainous) Neuralgia and Its Treatment, Brit. M. J. **1**:457 (March 7) 1936.

and the accompanying sympathetic fibers.[20] I also employed this procedure, together with division of all nerves and blood vessels beneath the eyebrow, to give relief in cases of supraorbital postherpetic neuralgia.

Glaser and Beerman [21] analyzed 200 cases of atypical facial neuralgia. In 47 per cent the pain started in the upper jaw, the malar region and the nose and spread from these areas to the head and neck.

Livingston [22] in 1938 found it difficult in the cases of patients with fantom limb pain to apply the theory that the relief of peripheral nerve pain obtained by section of sympathetic fiber tracts might be due to some alteration of the blood supply acting on pain receptors of the somatic nerves, since in his patients there were no sensory end organs in the parts where the pain was felt to originate.

Larsell [23] stimulated the nasal mucosa and observed the blood vessels in the ear of the rabbit after first sectioning the maxillary nerve proximal to the sphenopalatine branches. After section of the cord between the sixth and the seventh cervical segment or of the cervical portion of the sympathetic trunk, vasoconstriction did not take place when the stimulus was applied. His interpretation of the results confirmed the work of Davis and Pollock and others.

Tinel [24] reviewed the sympathetic neuralgias but could offer no relief for those involving the face. He felt that there is a "sympathetic afferent path" that is latent and only capable of being awakened in certain pathologic states to transmit severe pain.

Money,[25] using the classification of Harris, reported cures by injection of alcohol into the gasserian ganglion for migrainous or ciliary neuralgia and relief in cases of sympathetic hemicrania from "right stellate ganglionectomy."

Fay [26] divided pain into (1) the sharp, stabbing, shooting, lightning-like, cramplike momentary pain characteristic of true neuralgias, indicating intrinsic involvement of the nerve or its roots; (2) the burning,

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20. Reichert, F. L.: Treatment of the Neuralgias of the Head and Face, Proc. Second Cong. Pan Pacific S. A., 1936, p. 183.

21. Glaser, M. A., and Beerman, H. M.: Atypical Facial Neuralgia: An Analysis of Two Hundred Cases, Arch. Int. Med. **61**:172 (Feb.) 1938.

22. Livingston, W. K.: Fantom Limb Pain: A Report of Ten Cases in Which It Was Treated by Injection of Procaine Hydrochloride near the Thoracic Sympathetic Ganglions, Arch. Surg. **37**:353 (Sept.) 1938.

23. Larsell, O.: The Sympathetics of the Head, West. J. Surg. **46**:633 (Dec.) 1938.

24. Tinel, J.: Les algies sympathiques, Arch. internat. de neurol. **57**:1 (Aug.); 1 (Sept); 1 (Oct.) 1938.

25. Money, R. A.: Neuralgias of Cranial and Cervical Origin Other Than Tic Douloureux, Australian & New Zealand J. Surg. **8**:356 (April) 1939.

26. Fay, T.: Problems of Pain Reference to the Extremities: Their Diagnosis and Treatment, Am. J. Surg. **44**:52 (April) 1939.

scorching, tingling pain associated with causalgias, indicating compression, mild traumatic injury or constriction by adhesions along the nerve or its roots, and (3) dull, aching, throbbing, boring, pressure-like pain indicative of vascular pain and associated with some distention or stretch of the arterial and capillary network of vessels. He expressed preference for chordotomy of the anterolateral column for pain along the vascular pathway in the extremities but did not discuss the treatment of vascular pain in the face or head.

Thus, in the past thirty years attention has been kept focused on the unusual facial pains. The recent attempts to subdivide the large group of atypical facial neuralgias have permitted the development of therapeutic procedures that offer relief in a majority of cases. During the past fifteen years the autonomic nervous system has been implicated in these atypical facial neuralgias, and its role in the production of pain has led to important clinical and experimental observations.

BUCCAL NEURALGIA

Buccal neuralgia, a form of atypical facial neuralgia, is characterized by a burning, boring, aching, throbbing, toothachy pain in the region of the lip, cheek, gum, tongue, maxilla, nose, upper jaw and sometimes lower jaw, spreading at times to the zygoma, into or behind the eyeball or to the temporal region. It may be present for minutes to hours to days, with exacerbations of sharp, stabbing pain. Light touch to the involved part rarely starts an attack, but chewing, talking, local pressure or cold frequently induces an exacerbation. Hypersensitiveness to pressure over the carotid, facial and temporal vessels is frequently elicited. Extraction of teeth and injection of alcohol into the branches of the trigeminal nerve gave no relief. A few patients with hypothyroidism were relieved by thyroid extract and vitamin B. The majority of others were relieved by either alcoholic block of the cervicothoracic sympathetic ganglions or by resection at the lower border of the mandible of the facial artery, vein and sympathetic fibers.

ANATOMY

Not only were sympathetic fibers found on the facial artery and vein at operation, but from one to four rather large sympathetic fibers were resected in the soft structures surrounding these vessels (fig. 2).

Anatomic dissection of the sympathetic fibers in the face was rather difficult, but the semidiagrammatic drawing (fig. 1) shows the location and course of these fibers. To illustrate the numerous apparent anastomoses with the fibers of the seventh nerve in the cheek would be confusing, nor are the many small branches about the facial artery and vein indicated in the illustration. The main sympathetic fibers on

and accompanying the facial vessels course along the external carotid artery, where anastomoses are made with the fibers of the sympathetic trunk to the superior cervical ganglion and with fibers accompanying the temporal and occipital vessels, but the main group of fibers course downward to enter the carotid sinus at the bifurcation. The fibers from the carotid sinus pass downward along the great vessels of the neck to enter the cord at the seventh cervical and the first and second thoracic segments.

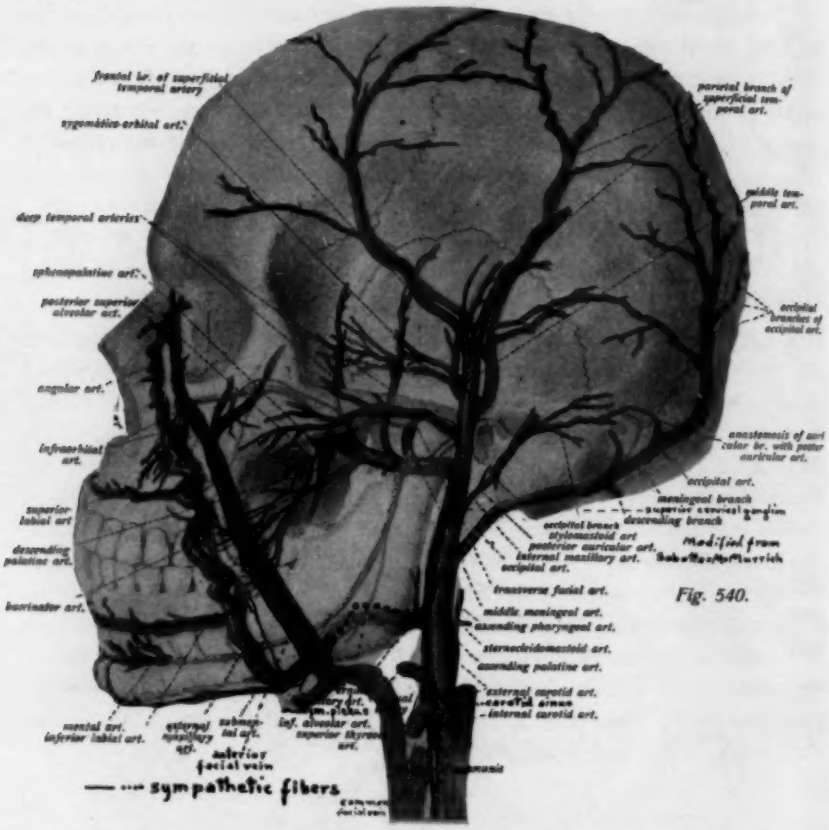

Fig. 540.

Fig. 1—Semidiagrammatic representation from anatomic dissection of sympathetic fibers accompanying the arborizations of the facial artery and vein from the carotid sinus at the bifurcation of the common carotid artery. (Modified from a drawing in Sobotta, J.: Atlas and Textbook of Human Anatomy, edited with additions by J. P. McMurrich, Philadelphia, W. B. Saunders Company, 1907, vol. 3.)

These anatomic findings on the course of the sympathetic fibers in the face seem to confirm the interesting experiments of Fay [13] when he stimulated (with the region under local anesthesia) the vascular tree in the neck of the human being.

That the sympathetic fibers in the face are involved in buccal neuralgia seems evident from anatomic and clinical study, but no contribution has been made as to the mechanism of the pain. It was noted, however, in some patients that after resection of the sympathetic fibers accompanying the facial vessels an occasional pain was felt but gradually disappeared in from one or two days to three weeks.

TREATMENT

Surgical treatment for buccal neuralgia by dividing the facial vessels and the sympathetic fibers developed from the observations made in case 1 in 1929 and was first employed in 1932. Previously, in a majority of cases relief had been secured by the more difficult and extensive procedure of injection of alcohol into the cervicothoracic sympathetic ganglions.[27]

The division of the sympathetic fibers along with the facial artery and vein is a simple procedure which does not produce Horner's syndrome or the troublesome alcoholic neuritis that appears after interruption of the cervicothoracic portion of the sympathetic chain.

With the region under local anesthesia an incision 2 to 3 cm. long, parallel to and just below the lower border of the mandible, is made over the facial artery as it comes around the lower edge of the jaw (fig. 2). A resection (with ligation) of 1 cm. of the facial artery and facial vein, as well as of the contiguous soft parts containing sympathetic fibers, is made. The ends of the divided structures retract over the lower border of the jaw, preventing regeneration.

CLINICAL MATERIAL

Of the 30 patients seen during the past ten years that belong in the group classified as having buccal neuralgia, 1 patient, receiving no treatment, had spontaneous relief. Three other patients with hypothyroidism secured relief from administration of thyroid extract and vitamin B. Of 8 patients treated by alcoholic block of the cervicothoracic portion of the sympathetic chain, 5 were relieved at once of their neuralgia; 2 obtained no relief, and 1 had temporary relief. Division of the facial artery, vein and sympathetic fibers was performed in 17, and 13 were relieved of their neuralgia. Three were not helped by the operation, and questionable relief was secured in a "mental case." In 1 patient with limited buccal or angular neuralgia, relief was obtained by division of the angular artery, vein and sympathetic fibers. Ten patients had an associated tic douloureux of one or more branches of the trigeminus nerve.

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27. Flothow, P. G.: Diagnostic and Therapeutic Injections of the Sympathetic Nerves, Am. J. Surg. **14**:591 (Dec.) 1931.

REPORT OF CASES

CASE 1.—Mr. O. C. M., aged 81, for twenty years had annual monthly attacks of burning pain, with frequent sharp stabs, in the right cheek and the lips, spreading to the zygomatic region. On examination, in February 1929, the right facial artery was tortuous and pulsated markedly. Its accidental occlusion by digital pressure at the angle of the jaw stopped the pain. When he returned, in October 1930, he stated that digital compression of this artery had given satisfactory relief during the last attack. No reply was received to a letter sent in January 1940.

CASE 2.—Mrs. H. R., aged 27, had a burning, aching pain in the left side of the upper jaw and gum, spreading to the tongue and eye, which had been present for fifteen months. Cocainization of the sphenopalatine ganglion and injection of alcohol into the maxillary branch of the trigeminus nerve in April 1930 gave no relief. Her pain stopped spontaneously in September 1931.

CASE 3.—Mrs. S. K., aged 58, had true tic douloureux of the left maxillary branch of the trigeminal nerve and a constant burning, aching pain in the left cheek, upper and lower jaw and the base of the tongue which were present for over a year. In April 1931 injection of alcohol into the lower two branches of the trigeminus nerve gave complete relief of the tic pain, but the burning, aching pain was not stopped until the sympathetic ganglions at the seventh cervical and the first and second thoracic segments were treated with injections of alcohol. It was reported that she remained well until her death in Japan in 1937.

CASE 4.—Mrs. M. C., aged 48, underwent intracranial section of the right trigeminal root in September 1929 for ticlike pains in the second and third branches of the nerve. In July 1931 she returned because of burning, scalding pain in the right cheek, tongue and lips, with aching in the zygomatic and maxillary regions. Injection of alcohol into the cervicothoracic portion of the sympathetic chain on the right gave relief up to the time of the last report, in February 1932.

CASE 5.—Mrs. G. B., aged 27, with a toothachy pain in her left jaw and cheek, spreading to her eye, was relieved in September 1931 by a paravertebral alcoholic block of the cervicothoracic sympathetic fibers. Neuralgia referable to the left geniculate ganglion developed in 1934. She reported in February 1940 that she had had no facial pain since treatment in 1931.

CASE 6.—Mr. A. B., aged 40, suffered at intervals for fifteen years with ticlike pains in the right side of the face, as well as a boring, aching pain in the right cheek, spreading to the eye and ear. Injection of alcohol into the right second branch of the fifth nerve in October 1931 gave relief until February 1932, when another injection was performed, but the boring, aching pain in the cheek persisted until relieved by injection of alcohol into the sympathetic chain at the seventh cervical and the first and second thoracic segments. This cervicothoracic portion of the sympathetic chain was removed surgically in September 1936, when the buccal neuralgia returned. Since then the patient has been free of buccal neuralgia, but reinjection into the maxillary branch was done in November 1939.

CASE 7.—Mrs. A. R., aged 35, experienced neuralgia referable to the left geniculate ganglion, with aural herpes and palsy of the facial nerve in February 1930, followed by an attack on the right side with palsy of the nerve on that side in May 1930. These attacks left a residual pain, consisting of severe aching in the left cheek and in the jaws and ear. Injection of procaine hydrochloride into the left cervicothoracic sympathetic fibers gave temporary relief in September 1931 and again in November 1932. The patient died of uremia in January 1933.

CASE 8.—Mrs. M. N., aged 52, in November 1931 complained of burning pain in the right cheek, tongue and zygoma, spreading to the eye. This was relieved by alcoholic block of the cervicothoracic sympathetic fibers on the right until February 1932. Elsewhere the trigeminal root was cut in 1937, and the facial vessels and sympathetic fibers were divided in 1938, without relief. She still suffers from buccal neuralgia.

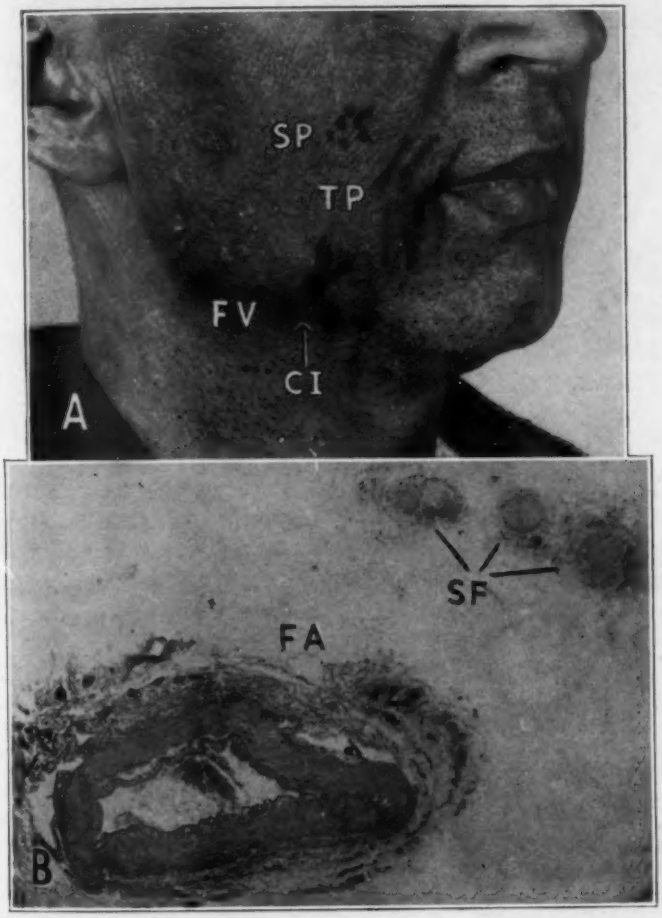

Fig. 2 (case 9).—*A*, cutaneous incision indicated for division of the facial artery, vein and accompanying sympathetic fibers. *SP* represents stabbing pain; *TP*, trigger point; *FV*, facial vessels, and *CI*, cutaneous incision. *B*, photomicrograph showing many small sympathetic fibers in the tissue surrounding the wall of the facial artery, as well as three larger sympathetic fibers in the tissue adjacent to the facial vessels. *SF* represents sympathetic fibers; *FA*, facial artery.

CASE 9.—Mr. L. W., aged 40, for over a year suffered from an aching, throbing pain in the region of the upper right first molar, followed by a burning pain in the gum and upper jaw. Talking, eating and movement of the lips would induce the

attacks. Compression of the right facial artery immediately stopped the pain. In January 1932, with the region under local anesthesia, the facial artery, the vein and the accompanying sympathetic fibers were resected. Three large sympathetic fibers and numerous smaller ones in the loose tissue about the walls of the vein and artery were observed on histologic study (fig. 2). An occasional stab of pain persisted for two weeks after operation. As recently as February 1940 an occasional stab would be experienced at weekly or bimonthly intervals.

Case 10.—Mr. G. W., aged 49, in May 1932 complained of a ticlike pain intermittently present on the right side for four years. Recently a burning, boring pain in the right upper jaw and cheek had developed. Alcoholic block of the right cervicothoracic sympathetic fibers in May 1932 and again in August 1935 cured the buccal neuralgia. On Feb. 7, 1940, Horner's syndrome was still present, and a fourth injection of alcohol into the second and third branches of the trigeminus nerve was made to relieve the recurrent tic douloureux.

Case 11.—Mrs. M. B., aged 55, had the sensory root of the trigeminus nerve divided in 1930 by K. McKenzie[28] for tic douloureux. Recent burning, crawling sensations in the left cheek and aching of the maxilla were only temporarily stopped by injection of alcohol into the cervicothoracic ganglions. In May 1933 excision of the left carotid sinus gave temporary relief. In February 1940 the pain was still present in spite of recent injections and operations on the sinus.

Case 12.—Mrs. B. E. M., aged 65, had terrific burning pain over the left side of the forehead, in and behind the eye and along the cheek to the maxilla and nostril, following a supraorbital herpes zoster four months before. An incision through the left eyebrow, dividing all the nerves and blood vessels together with the sympathetic fibers and a second incision for division of the left facial artery, vein and sympathetic fibers gave complete relief of all pain except slight aching behind the eyeball. This relief extended from October 1935 until death in 1937.

Case 13.—Mrs. E. K., aged 62, underwent excision of the facial vessels and sympathetic fibers on the right in July 1936 for aching pain in the cheek and temporal region associated with attacks of stabbing pain in the same area. She has had no return of buccal neuralgia to date.

Case 14.—Mrs. H. L. C., aged 67, had spells of burning, aching pain in the right cheek and nose, spreading to the eye and ear. When given thyroid extract and vitamin B in September 1936 she obtained relief within two weeks and had remained well to February 1940.

Case 15.—Mr. F. A. B., aged 49, had frequent sharp pains in the upper left bicuspid for six years, associated with dull, aching pain in the left cheek, lip and nostril. In September 1936 the facial vessels and sympathetic fibers on the left were divided, with complete relief, which continued to the last report (October 1939).

Case 16.—Mrs. G. E. H., aged 43, was seen in October 1936 for burning pain in the right cheek, jaw and nose associated with stabs of pain in the upper lip and nasolabial fold. She was found to have hypothyroidism. Thyroid extract and vitamin B gave relief until she stopped treatment, in the fall of 1939. Relief was again secured on resuming medication.

Case 17.—Mrs. S. E. S., aged 62, suffered for four years from ticlike pain in left upper jaw and lip, as well as dull, aching pain in the left cheek and maxilla.

28. McKenzie, K. G.: Observations on Results of Operative Treatment of Trigeminal Neuralgia, Canad. M. A. J. **29**:492, 1933.

In October 1936 injection of alcohol into the maxillary branch cured the tic pain, but the buccal neuralgia persisted until resection of the facial vessels and sympathetic fibers. The last report, in February 1940, stated that she had remained free of buccal neuralgia since operation and from the tic pain since reinjection in February 1939.

Case 18.—Mr. E. C., aged 48, at intervals for twenty years experienced a constricting, aching pain in the left cheek, gums and upper teeth, spreading to the nose and behind the left eye. He has remained free of pain since division of the left facial vessels and sympathetic fibers in November 1936.

Case 19.—Mr. F. W. W., aged 66, had ticlike pain in the left upper lip cured by injection of alcohol into the infraorbital nerve in February 1937, but a severe burning, aching pain in the left side of the face and upper lip was not relieved until the facial vessels and sympathetic fibers were divided a month later. Only a return of the tic pain was reported in February 1940.

Case 20.—Mr. J. M., aged 80, had a constant dull pain in the upper left gums and cheek which was not cured by injection of alcohol into the second and third branches of the trigeminus nerve and only temporarily relieved by division of the left facial vessels and sympathetic fibers in September 1937. He was committed to an institution because of disorientation and delusions of grandeur.

Case 21.—Mr. J. H. R., aged 65, had a hammerlike pain in the left upper lip and upper jaw, extending to the tongue and cheek. Division of the facial vessels and sympathetic fibers in March 1937 gave relief until his death, in May 1939. In October 1937 a ticlike pain in the upper gums on the left was relieved by injection of alcohol into the maxillary branch.

Case 22.—Mrs. A. J. M., aged 80, complained of a constant dull ache in the right angle of the mouth, spreading to the cheek and eye. A trigger point was found at the corner of the mouth. In January 1938 the facial vessels and sympathetic fibers were divided, affording temporary relief. She did not return for further treatment.

Case 23.—Mrs. B. T. R., aged 46, had aching pain in the lower jaw, spreading to the left cheek and the zygoma for five years. Division of the facial vessels and sympathetic fibers in March 1938 and injections of procaine hydrochloride into the dental nerve and into the gums gave no relief, nor did thyroid extract and vitamin B.

Case 24.—Mr. C. E. C., aged 43, has remained relieved of aching, burning pain in the left cheek and maxilla since division of the left facial vessels and sympathetic fibers in April 1938.

Case 25.—Mr. A. H., aged 62, had stabbing, throbbing, burning pain in the left cheek and jaws for five years. In April 1938 division of the facial vessels and sympathetic fibers on that side relieved the burning pain in the cheek, but the stabbing, throbbing pain persisted until alcoholic block of the mandibular branch of the fifth nerve. Return of the stabbing pain in August 1939 was relieved by reinjection into the mandibular branch.

Case 26.—Mrs. E. F., aged 62, had alcohol injected into the right maxillary nerve in April 1938 for stabbing pain in the right cheek. In January 1939 a burning, throbbing pain in the right cheek appeared, which has not returned since division of the facial vessels and sympathetic fibers.

CASE 27.—Mrs. L. C., aged 46, in January 1939 complained of nocturnal sharp aching pains in the right cheek, eye and upper jaw, which have been relieved by correcting her hypothyroidism with thyroid extract and vitamin B.

CASE 28.—Mrs. M. G. D., aged 61, had attacks of burning pain in the left cheek, jaws and nose, spreading to the tongue. In March 1939 division of the facial vessels and sympathetic fibers on the left gave complete relief. There has been no report on the patient since April 1939.

CASE 29.—Mrs. H. M., aged 57, suffered from attacks of aching, burning pain in the left cheek for sixteen years. Since division of the facial vessels and sympathetic fibers on that side in December 1939 she has experienced only an occasional pain in the cheek, with many intervening days when she is entirely free of pain.

CASE 30.—Mr. W. E. G., aged 59, had severe aching pain for a year in the left angle of the jaw seven years ago. Four years ago sharp pains followed by a burning, aching pain started in the inner angle of the lower left eyelid and extended down to the nasolabial fold and to the cheek. Injection of procaine hydrochloride into the infraorbital nerve gave no relief, but injection about the angular artery stopped all pain. In January 1940 excision of the left angular artery, vein and accompanying sympathetic fibers gave complete relief, which has continued to the last report (March 1940).

SUMMARY

Buccal neuralgia, a form of atypical facial neuralgia, is characterized by a burning, boring, aching, throbbing pain in the region of the lip, cheek, gum, tongue, maxilla, nose, upper jaw and sometimes lower jaw, spreading at times to the zygoma, into or behind the eyeball or into the temporal region.

Anatomic dissection demonstrated sympathetic fibers from the carotid sinus following the arborizations of the facial artery and vein.

Extraction of teeth and injection of alcohol into branches of the trigeminal nerve gave no relief.

A report is made of 30 patients suffering from buccal neuralgia.

Tic douloureux of one or more branches of the trigeminus nerve was associated with buccal neuralgia in 10 patients.

Three patients with buccal neuralgia exhibited hypothyroidism. The neuralgia was relieved by administration of thyroid extract and vitamin B.

Buccal neuralgia was cured in 5 of 8 patients in whom the cervicothoracic portion of the sympathetic chain was interrupted.

Buccal neuralgia was relieved in 13 of 17 patients by the simpler procedure of division of the sympathetic fibers with the facial artery and vein at the lower border of the mandible.

MICROSCOPIC CHANGES INDUCED IN THYROID GLAND BY ORAL ADMINISTRATION OF DESICCATED THYROID

USE OF THE SUBSTANCE IN TREATMENT OF CONGENITAL AND SIMPLE COLLOID GOITER

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The first demonstration of the effect of a substance from outside the body on the microscopic structure of the thyroid gland was the deposition of colloid within the follicles of the thyroid gland of the dog after the administration of iodine, reported by des Ligneris [1] in 1907 and by Marine and his co-workers [2] in 1908. Since these early observations there have appeared in the literature from time to time controversial reports regarding the effects of iodine and other substances on the normal thyroid as well as on certain types of enlargement of the gland, (Loeb [3] and others [3a]). It would be aside from the purpose of this paper

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1. des Ligneris, M.: Experimentelle Untersuchungen über die Wirkung des Jods auf die Hundesschilddrüse, sowie über die Hyperplasie dieser Drüse, Berne, Rösch & Schatzmann, 1907.

2. Marine, D., and Williams, W. W.: The Relation of Iodine to the Structure of the Thyroid Gland, Arch. Int. Med. **1**:349-384 (May) 1908.

3. Loeb, L.: The Structural Changes Which Take Place in the Thyroid Glands of Guinea Pigs During the Process of Compensatory Hypertrophy Under the Influence of Iodine Administration, Endocrinology **13**:49-62 (Jan.-Feb.) 1929.

3a. Webster and Chesney administered iodine in the form of compound solution of iodine U. S. P. to 10 rabbits with hyperplastic goiters and observed rapid loss of weight, marked increase in heat production and death of the animal in most instances (Webster, B., and Chesney, A. M.: Endemic Goiter in Rabbits: III. Effect of Administration of Iodine, Bull. Johns Hopkins Hosp. **43**:291-308, 1928). They stated that "in every instance in which the animal survived the iodine administration for more than one week, a decrease in the size of the goiter was noted." Microscopic sections of the thyroid glands of the animals showed hyperplastic goiters in various stages of involution, and the degree of involution was directly proportional to the length of the period during which iodine was administered. The behavior of these animals suggested to the authors that after administration of iodine an excess of thyroid secretion had suddenly been elaborated and poured into the circulation. It was as if the thyroid glands in these animals had been

(Footnote continued on next page)

to attempt a critical résumé of the vast literature on this subject up to the present, for, although there have been many and important contributions to knowledge of enlargement of the thyroid gland, the cause and method of prevention of all types of goiter remain unsolved problems.

In all probability the goitrogenic factors vary in different parts of the world and particularly in various regions of the United States of America. Similarly, enlargement of the thyroid in certain localities will not only differ in extent but may show structural and microscopic changes varying from typical simple colloid goiter to goiter composed of small follicles which are poor in colloid. There will be found all gradations between these two distinct types, at times not only in the same locality but also in the same person. Again, such an enlargement may present as a diffuse or as a nodular goiter.

It would seem, therefore, that the methods of prevention of goiter as well as those of treatment would differ, depending on the locality, the extent of the enlargement and the microscopic structure of the gland. The deletion or inclusion of specific dietary substances effective in certain types of goiter under one group of conditions may be totally ineffective in another situation, in which a different type of goiter prevails.

The object of this report is to call attention to the therapeutic effect of desiccated thyroid in cases of simple colloid goiter of the type encountered along the mid-Atlantic seaboard and to note the effects of this substance on the microscopic structure of the gland. In the hope that some light may be thrown on atrophy of the thyroid, the accumulation of colloid in the gland and the entire complex subject of goiter, these data are presented.

REPORT OF CASES

CASES 1 and 2.—In 1925 there appeared in the thyroid clinic of the Johns Hopkins Hospital dispensary 2 sisters aged 16 and 18, born in the United States of an American mother and a Swiss father. There was no instance of goiter on the maternal side of the family, but the father and the paternal grandparents were all affected with it. The 2 girls had been afflicted with large goiters since their birth in Baltimore, a nongoitrous area. They were, in addition, somewhat dwarfed compared with other girls of their age. Their facies and mental retar-

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rendered capable of synthesizing large amounts of thyroid secretion if the proper elements were available and did so as soon as iodine was supplied. In support of this view was the authors' observation that the severity of the reaction following the administration of iodine was proportional to the degree of hyperplasia present in the gland. Dr. Chesney, in a personal communication to me, has suggested that these hyperplastic thyroids might have elaborated a substance which was a precursor of thyroxin and that the administration of iodine served to convert this hypothetic substance into the active molecule, thus flooding the animal, so to speak, with an excess of the secretion of the thyroid gland.

dation were typical of a marked degree of hypothyroidism and in 1, the younger, immature congenital cataracts were present. Compound solution of iodine U. S. P. in rather large doses (10 cc. every day) had been given to both of them over a period in excess of two years, without beneficial results. On the contrary, there had in this time been a further enlargement of the thyroid. The basal metabolic rates on admission to the clinic were —26 per cent and —36 per cent respectively. For a number of months, while the iodine therapy was continued, these patients were kept under close supervision in the thyroid clinic. After repeated examinations, during which measurements were made of their enlarged thyroids, administration of iodine was stopped. In fact, not only did their clinical condition fail to improve as a result of administration of iodine, but the manifestations of hypothyroidism had become accentuated, and the goiters were increased not only in size, but in consistency. The increase in consistency produced an unpleasant sense of rigidity in the neck, especially when the patients lay in the recumbent posture.

On account of the low basal metabolic rates an attempt was made to relieve the marked functional deficiency of the thyroids by oral administration of tablets of desiccated thyroid. In a few weeks the dose was increased from 1 to 3 grains (0.06 to 0.19 Gm.) per day, and as the basal metabolic rates mounted the thyroid glands began to diminish in size. After three months there was by actual measurement a return of the thyroids to almost the normal size, but there was still a considerable increase above normal in the consistency. After six months, during which 3 grains (0.19 Gm.) of thyroid was given every day, there remained no visible evidence of goiter, and unless the rather pronounced induration of the thyroids was felt the abnormality in the glands would have remained unsuspected. The patients were clinically much improved, and their basal metabolic rates were restored to within normal limits. The younger was later successfully operated on by Dr. Alan C. Woods for bilateral cararacts, while the other was treated in the psychiatric outpatient department as an "intellectual inferior." After a few years they moved away, their destination unknown.

Case 3.—Some time later a newborn infant was admitted to the pediatric department of the Johns Hopkins Hospital suffering from severe dyspnea, cyanosis and a pronounced enlargement of the thyroid gland, present at birth. In view of our previous experience, thyroxin was given hypodermically, with very rapid amelioration of the respiratory difficulties and a demonstrable reduction in the size of the gland after a few days. The thyroid within some months was restored to a relatively normal size. Experience has demonstrated beyond question that in infants with such conditions iodine is totally inefficacious and surgical procedures very hazardous.

Case 4.—J. L. E., a boy 11 years of age, had diffuse goiter with hypothyroidism. The boy was also observed in the Harriet Lane Home in consultation with Dr. Lawson Wilkins. The mother was operated on for an enlarged cystic thyroid gland slightly before the birth of this, her only child. At the age of 2½ years a prominent enlargement of the thyroid gland developed, which increased in size each year. The attending pediatrician, Dr. Robert Strong, concluded that the patient had a diffuse colloid goiter with hypothyroidism and gave the child iodine by mouth, which caused an increase in the size as well as in the consistency of the gland. The boy was then given 2 grains (0.13 Gm.) of thyroid by mouth each day, with an early improvement not only in his mental status and alacrity but in his physical activities. At the time of this report the

thyroid therapy has been continued for nine years, during which time the child has developed mentally and physically in a normal manner. On occasions the thyroid has been temporarily discontinued. On all such occasions it is said the thyroid gland becomes much larger. He usually gains weight rapidly, at times as much as 11 pounds (5 Kg.) in two months. He also becomes sluggish and irritable. The basal metabolic rate decreases rapidly, and the enlargement of the thyroid becomes more pronounced. In order to estimate the extent of his hypothyroidism all thyroid therapy was discontinued. In a few weeks the boy gained

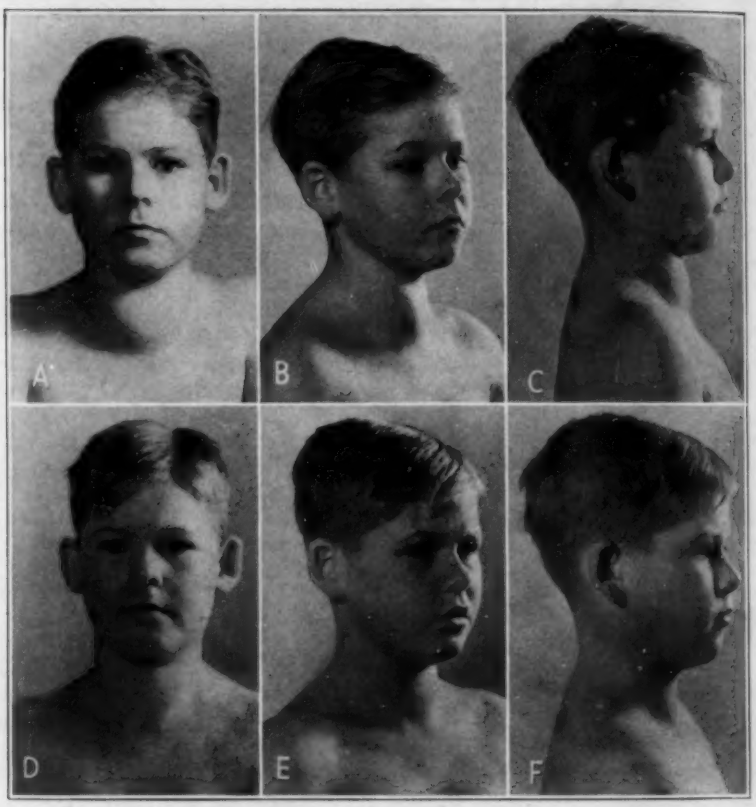

Fig. 1.—*A*, J. L. E., showing the presence of a colloid goiter before oral administration of thyroid. *B*, semiprofile view. *C*, profile view. *D*, J. L. E. after eight weeks of treatment with 3 grains (0.19 Gm.) of thyroid per day. Compare with *A*; note the disappearance of the goiter, due to atrophy of the thyroid gland. *E*, semiprofile view; compare with *B*. *F*, profile view; compare with *C*.

weight rapidly (8 pounds [3.6 Kg.]); the abdomen became protuberant, and he became mentally sluggish as well as irritable. The thyroid gland increased in size each week. After two months the clinical manifestations of hypothyroidism were pronounced, and a marked enlargement of the thyroid gland was evident (fig. 1, *A*, *B* and *C*). On palpation the gland was diffusely enlarged to about four or five times the normal size and much decreased in consistency. It was

similar in all clinical respects to a simple diffuse colloid goiter. The basal metabolic rate was —18 per cent, and the value for blood cholesterol was 206 mg. per hundred cubic centimeters. Three grains (0.19 Gm.) of thyroid was then given by mouth each day, and in two months the physical status, the weight, the mental activities, the general briskness and the metabolic processes, i. e., the basal metabolic rate and the level of blood cholesterol, had all returned to normal. Although the thyroid gland could be palpated, it was of normal size and consistency, more dense than before but much smaller. The fluctuations in size of the thyroid gland after discontinuance of the thyroid therapy with an interval, i. e. two months, before it was again administered were remarkable (fig. 1, *D*, *E* and *F*).

Case 5.—In the fall of 1930 L. K., a married woman aged 30, was admitted to the Church Home and Infirmary complaining of goiter, choking sensations, difficulty in swallowing, shortness of breath, nervousness, poor appetite and loss of weight. The patient was born and reared in Thurmont, a few miles from Baltimore, in the flat, nonmountainous district of western Maryland. She had had an enlargement of her thyroid gland as far back as she could remember, but her general health had been excellent. The enlargement of the thyroid was a constant source of embarrassment to her. Her family and friends frequently made remarks concerning the gradual increase in the size of her goiter over a period of years. She had been married at the age of 24 and had one child. The size of her thyroid increased markedly during pregnancy and even more after her child was born. She had always felt sluggish, with practically no animation, and stated that her physician constantly told her that she had a very low blood pressure. Her hair, always dry, of late had been falling out. She was habitually slightly overweight; her eyes were somewhat puffy, and she had a tendency to gain weight even though her appetite was never good. Her pulse was usually slow. She had not been conscious of her heart beat. She rarely felt the heat and in the winter was cold almost constantly. Of late, however, she had become nervous about her goiter because, in spite of the fact that she had taken rather frequent and large doses of iodine in the form of compound solution of iodine U. S. P. by mouth for over two years, it was her impression that there had been no diminution in the size of her goiter but that, on the contrary, it had actually increased. She had estimated this increase by her own impression and by that of her friends and family as well as that of her family physician and also by the fact that she had experienced difficulty in breathing at times.

The patient was admitted to the hospital for examination and a study of the functional status of her thyroid gland. Physical examination gave essentially negative results except that the hair and skin were dry and the face somewhat puffy, particularly under the eyes. The subcutaneous tissue generally seemed to be thicker, as if there were some subcutaneous edema. There were no signs of hyperthyroidism. On inspection the thyroid gland was obviously enlarged to several times its normal size. This enlargement on palpation was revealed to be diffuse. The gland was soft. There were no nodules or tumors. The consistency of the parenchyma seemed to be definitely decreased below that of a normal thyroid gland. The impression obtained from examining this patient was unquestionably that of hypothyroidism resulting from or associated with diffuse soft colloid goiter. The basal metabolic rate was —10 per cent.

This patient was admitted for operative removal of a portion of the enlarged thyroid gland because medicinal (iodine) therapy had been totally ineffective. The thyroid gland under this form of therapy had increased not only in size but in consistency and was productive of more mechanical disturbance in this

hardened state than before the iodine was given. The question immediately arose as to what could be expected of further iodine therapy, whereupon it was generally agreed that the colloid already present in the gland under this form of treatment would probably become more dense and that more colloid would be deposited as a result of the administration of iodine. The possibility of intoxication due to the prolonged use of iodine must always be held in mind. In addition to this, the patient had lost her confidence in the probability that the iodine would bring about a reduction in size of the gland. An operative procedure to remove the enlarged gland for cosmetic reasons seemed illogical in the presence of the low basal metabolic rate already present, together with clinical signs of underactivity of the thyroid or of hypothyroidism. It was felt that further destruction of the thyroid gland would only increase the hypothyroidism and lead to additional untoward clinical manifestations. It was therefore decided to treat the patient by means of oral administration of thyroid tablets (Hynson, Westcott and Dunning), beginning with 1 grain (0.06 Gm.) a day and increasing the dose according to the condition of the patient and the changes noted in the basal metabolic rate. Before this type of therapy was instituted the matter was discussed thoroughly with the patient, and with her complete approval as well as understanding removal of a biopsy specimen from the thyroid with the region under local anaesthesia was decided on in order to determine the exact histologic characteristics of the gland. The patient had not taken iodine in any form for approximately six months before admission to the hospital, so it was felt that any effects of the iodine on the structure of the thyroid or on the organism as a whole would in a large measure, if not entirely, have disappeared. Accordingly, a small portion of the right lobe was removed for section. The thyroid gland in the gross seemed to be of uniform consistency, and the diagnosis of diffuse colloid goiter was unquestionably correct. The section of the gland taken before treatment with thyroid was studied and showed typical diffuse colloid goiter (figs. 2 and 3). A description of several sections of the tissue removed at the first biopsy follows. The histologic appearance was that of a simple colloid goiter. The follicles were everywhere filled with homogeneously staining colloid. The follicles differed in size but were, generally speaking, much larger than those seen in the normal human thyroid. The colloid abutted on the epithelium, which had been flattened out to almost the size of endothelial cells, much lower than the normal cubical epithelium usually encountered throughout the thyroid of the normal person. In places, even in this section, the pyknotic nuclei stood out in the cytoplasm like pearls in a necklace, the cytoplasm of the lining epithelium being apparently made scanty by increased intrafollicular pressure of the colloid. In some areas the epithelial cells could not be distinguished from the endothelial cells except for their position as a part of the lining of the follicle, their nuclei being flattened and the cytoplasm merely tapering off from this elliptic type of nucleus. Practically no secretion vacuoles were seen in the lumens of the follicles. The smaller ones, between the larger, in all probability represented terminal portions of follicles of equal size which had been sectioned at different levels and which if they had been reconstructed would in all probability have been as large as the average in the section. The largest follicles seemed to have been cut across through their diameters. Except for blood vessels and lymphatics there was practically no interfollicular tissue. There were no wandering cells, lymphocytic cells or small mononuclears. Occasional clumps of cells, which obviously were epithelial and represented the domes of the underlying follicles, could be observed between those follicles which contained colloid. The microscopic appearance of this section was therefore typical of a simple colloid goiter, with accumulation

of colloid in large distended follicles lined with an atrophic type of epithelium, the latter, in all probability, being produced in part by pressure atrophy. The microscopic appearance of the cells was everywhere one of relative inactivity, and from the histologic appearance there seemed to be an accumulation of secre-

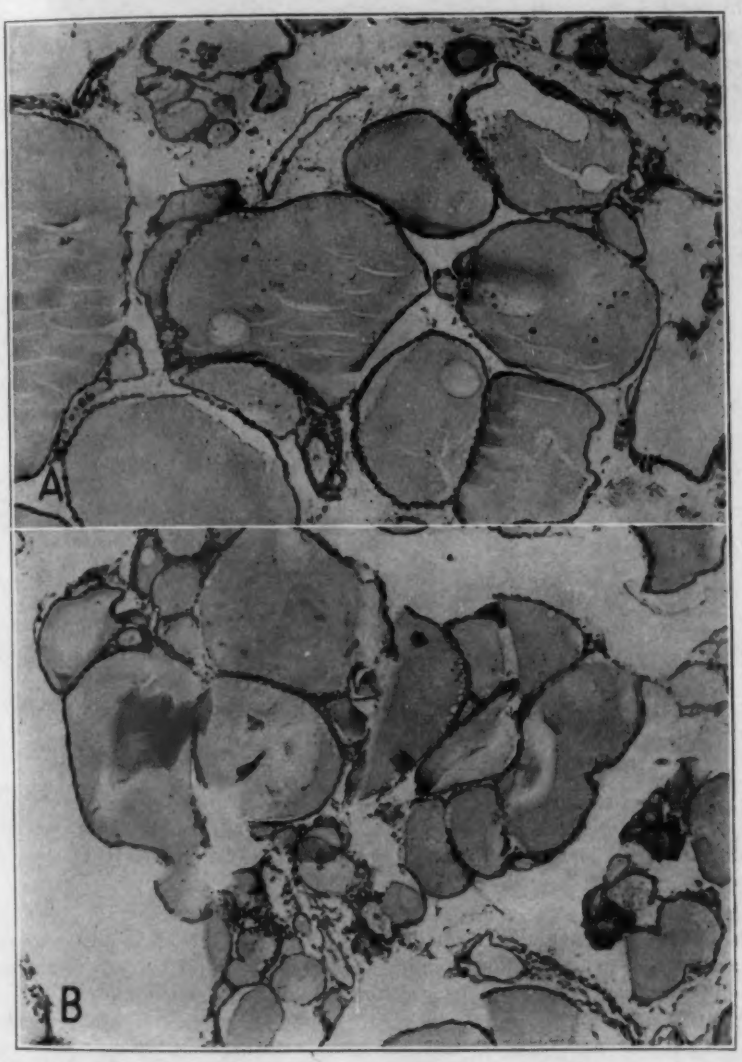

Fig. 2.—*A*, photomicrograph of a section showing typical simple colloid goiter (× 100; hematoxylin and eosin stain). The tissue was removed from the gland before oral administration of thyroid was instituted. Note the size of the follicles and the characteristics of the lining epithelium and the interstitial tissue. *B*, section (hematoxylin and eosin, × 100) of tissue removed for the first biopsy, as was that in *A*, but from another portion of the block.

tion, namely, the colloid, resulting from inability of this substance to escape into the blood stream. In other words, it appears that the gland, owing to its inadequate excretion, was ballooned out by its own secretion.

The patient was then given thyroid tablets (1 grain, or 0.06 Gm.) by mouth for one week. The dose was increased from 1 grain a day in the first to 2 grains (0.13 Gm.) a day in the second week; 3 grains (0.19 Gm.) a day in the second month, and up to 4 grains (0.26 Gm.) a day for the remaining four months of a six month period. This was increased by the patient on her own initiative to 6 grains (0.39 Gm.) a day for six months. It is to be noted that thyroid was administered first in October 1935. She returned April 15, 1936, at which time her basal metabolic rate had risen from —10 per cent to +11 per cent. During this period she had been taking 4 grains (0.26 Gm.) of thyroid a day. She had lost considerable weight and was feeling much better, and the gland had decreased

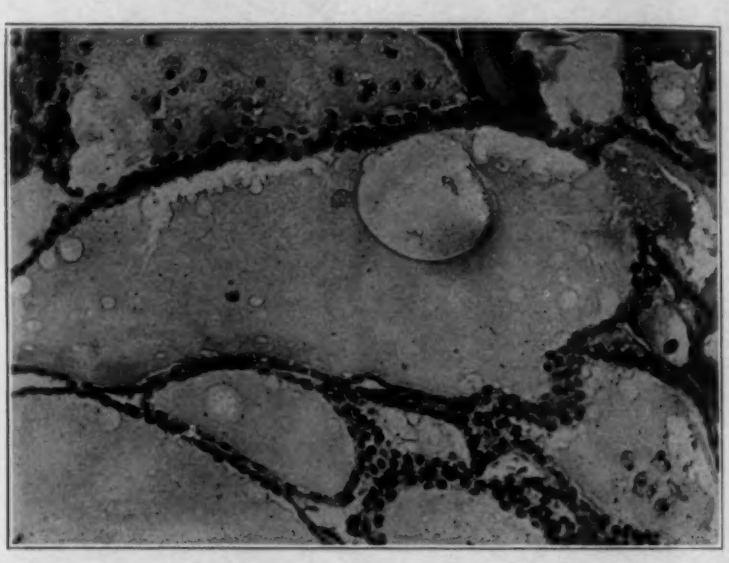

Fig. 3.—Photomicrograph of a high power field (hematoxylin and eosin, × 200) from the section shown in figure 2 *A*. The size of the follicles, the lining epithelium and the paucity of interstitial tissue are to be noted for comparison with subsequent figures.

markedly in size. She was mentally more alert, and her skin was somewhat oily and seemed to be of a finer texture. The falling out of her hair had ceased, and clinically she appeared to have distinctly less hypothyroidism.

It is interesting to note that during the first four or five months the patient stated that she was nervous, had palpitation and noticed some shortness of breath and increased fatigability. Later, although without seeking advice, she increased the dose of thyroid to 6 grains (0.39 Gm.) per day, after which the disagreeable symptoms of an excess of thyroxin in the circulating blood and tissues, i. e., nervousness, insomnia, palpitation, premature systoles, a sense of increased tremor and loss of weight, were not as prominent as when she had taken a smaller dose of thyroid, i. e., 3 to 4 grains (0.19 to 0.26 Gm.) per day. She had evidently established a tolerance for thyroid, and it had become less effective.

We have noted this tendency before and have felt that it is due not only to tolerance on the part of the patient but to atrophy of the thyroid gland with diminution of its secretion in the circulating blood caused by the exogenous supply of thyroid.

The patient then returned to her home, where she remained until Sept. 2, 1936, after taking thyroid in large doses for practically one year. At the end of this time she was readmitted to the Church Home and Infirmary, feeling much better than she had on the previous admission, although she was taking 6 grains (0.39 Gm.) of thyroid each day. She stated that she "felt her heart beat" somewhat more rapidly than before she had begun to take thyroid, but less so in the last four months. She was vigorous, did not sleep so much and on the whole felt that her condition had improved. She seemed to have a great deal more energy. The most striking feature was complete disappearance of the enlargement of the thyroid gland, or goiter. This was noticed by the same group of persons who had commented on the goiter previously, namely, her family, friends and family physician. Measurements of the neck made at the first and at this second admission also confirmed this observation. Examination at this time revealed a rather rapid pulse rate (running from 100 to 110), a perfectly regular pulse, an occasional premature systole, a well defined tremor of the extended fingers and a definite severity of expression, probably due to a retraction of the upper eyelids and a suggestive superior lid lag on rotation of the bulbs downward. The most interesting part of the examination centered around the thyroid gland. At this time the gland was not visible; the goiter had entirely disappeared. On palpation there was a small shrunken thyroid, markedly hardened and increased in consistency, entirely different to palpation from what it had been originally. In fact, it felt almost stony hard, like beginning Riedel's struma, and markedly diminished in size. It was as small as a normal gland, which corresponds to a diminution at least to one-fifth its pretherapeutic size. The basal metabolic rate at this examination was + 25 per cent, which was a total advance of 35 above the — 10 per cent noted on the patient's first admission to the hospital. On account of this marked elevation of the basal metabolic rate, which I thought was due to the hyperthyroidism induced by the patient's taking 6 grains (0.39 Gm.) of thyroid a day, and on account of the marked shrinking and hardening of the gland, another biopsy specimen was taken from a representative portion of the thyroid, definitely removed from the previous incision so that the microscopic appearance would not be interfered with by scar tissue from the previous removal. A small piece of tissue was thus removed, and photomicrographs of this are presented (figs. 4 and 5).

There was marked diminution in the number and size of the follicles (compare with figure 2 *A*), and there was also a paucity of colloid. That which was present stained homogeneously but somewhat deeply with eosin. One gained the impression that the colloid secretion remaining in the small and atrophic follicles was desiccated and hard. The great majority of the follicles were entirely empty or contained only a very small amount of colloid. They were decreased in size and number, while the intrafollicular stroma was everywhere strikingly increased. In some regions there appeared to be a large amount of substitution of fibrous tissue for parenchyma, giving the appearance of areas of broad scar formation. In other places there was a pronounced infiltration of small lymphocytic cells, which in some areas formed what appeared to be actual germinal centers similar to those described by MacCallum[4] as observed in the thyroid glands of patients with

4. MacCallum, W. G.: The Pathology of Exophthalmic Goiter, J. A. M. A. 49:1158-1162 (Oct. 5) 1907.

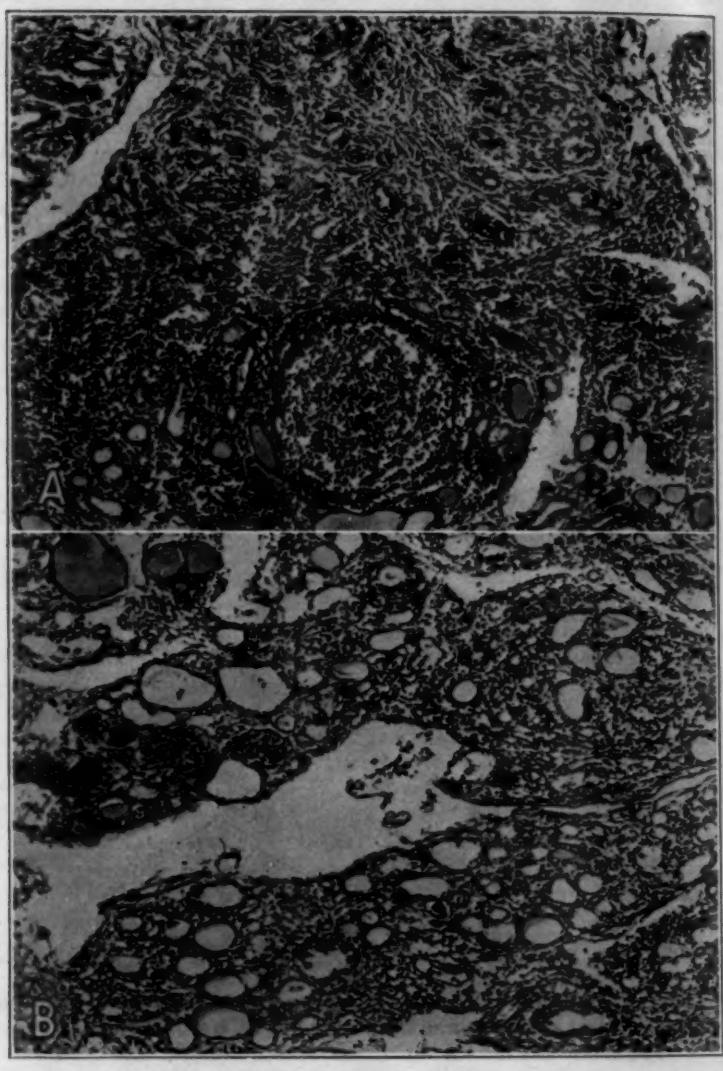

Fig. 4.—*A*, photomicrograph (hematoxylin and eosin, × 100) of tissue removed from the thyroid gland for the second biopsy, after oral administration of thyroid for one year. Compare with figures 2 and 3 (same patient). The thyroid parenchyma has undergone pronounced atrophy. Note the diminution in size and number of follicles and the apparent increase in interfollicular fibrous tissue, together with the infiltration of small lymphocytes. Germinal centers (originally described by MacCallum) are seen at the lower portion of the section. For complete description, see text. *B*, photomicrograph (hematoxylin and eosin, × 100) of a section from a different portion of the same block. The follicles are small; the majority are empty, and the colloid present is desiccated. There is infiltration with small lymphocytes. The epithelial cells are clear except for pyknotic nuclei. The eosin-staining protein content of the cytoplasm seems to have disappeared.

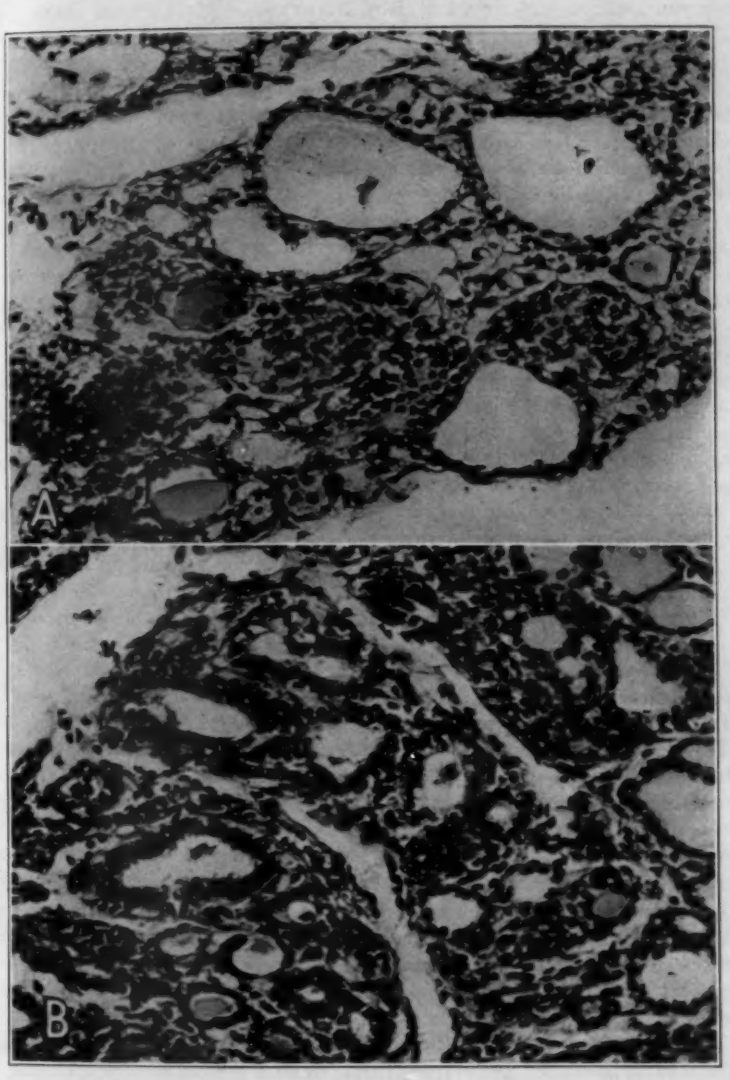

Fig. 5.—*A*, high power photomicrograph (hematoxylin and eosin, × 200) of the section shown in figure 4 *B*, demonstrating more clearly the empty follicles and the clear cytoplasm of the epithelial cells. The photomicrograph also shows that the interfollicular stroma is to a large extent composed of masses or cordons of epithelial cells derived from the collapsed, empty follicles. *B*, high power photomicrograph (hematoxylin and eosin, × 200) of a section of the same block shown in figure 4 and in *A*, demonstrating the contracture of the follicles to very small vesicles or even to such an extent that their lumens are obliterated so that the appearance of the section is that of a solid cord of epithelial cells.

exophthalmic goiter. It is interesting to note that in this instance also the patient, being stimulated by oral administration of thyroid, was in a state of clinical hyperthyroidism. Although there were many clusters of epithelial cells, which seemed to adhere to no particular pattern, the follicles which could be made out clearly were markedly reduced in size, containing a desiccated-appearing colloid or (as in the majority of instances) seeming to be entirely empty. They were lined with epithelium which consisted of very low cuboidal cells, the cytoplasm of which was almost colorless or took only a faint eosin stain. The protein content of the cells seemed to be much diminished; in some there was a cytoplasm that was atrophic but took a pink eosin stain fairly well. The nuclei were shrunken and pyknotic in the majority of cells and were irregular in shape; in some they were perfectly flat like endothelial cells. No secretory vacuoles were noted. There were entire areas of epithelial cells which stood out mainly by virtue of the nature of the pyknotic nuclei. These cells appeared as empty spaces surrounded by a thread-like wall. In some areas these cells were radially arranged, often with their apexes touching and in such close contact that no lumen in them could be seen. They merely made up cordons of atrophic epithelial cells and generally created the appearance of a large increase in the interfollicular stroma. In other places, rather large follicles in which the lining cells were absolutely colorless predominated. The lining cells looked almost like foam cells. There was generally an infiltration of the stroma with small lymphocytes around and between the large and empty follicles. Unless one had observed very closely the impression might have been obtained that there were large areas of scar formation, but these were made up in the main by small follicles from which the colloid had been absorbed and which, as a result, had shrunk down to become an almost solid cord of perfectly colorless cells. In other places there apparently was a definite increase, at least a relative one, in the pink-staining (eosin) white fibrous connective tissue. The gland had everywhere the appearance of disuse atrophy with the colloid secretion markedly decreased; that which was present before the excretory demands were so lowered (owing to the exogenous thyroid) had been absorbed. On account of the oral administration of thyroid the parenchyma of the gland had undergone true disuse atrophy rather than destruction of tissue. The areas that seemed to be scar may have been due merely to shrinking of the parenchyma, that is, the absence of colloid-containing follicles between normally placed and normal-sized fibrous connective tissue septums. The last-mentioned structures, owing to the relative shrinkage of the follicles, stood out much more prominently.

On account of the elevation of the basal metabolic rate and the clinical suggestion, particularly the ocular signs, of slight but definite hyperthyroidism, together with the microscopic appearance of atrophy of the thyroid gland, the patient was discharged to return and was told to discontinue all medicinal therapy. No thyroid or iodine in any form was administered, and particular attention was paid to the table and cooking salt to be sure that no iodized salt was ingested.

The patient remained away from the hospital for four months. During this period her nervousness entirely disappeared, as the thyroid had been discontinued. On her readmission to the hospital, although she seemed perfectly normal from the standpoint of her history and physical condition, the basal metabolic rate had dropped to —15 per cent on Jan. 18 and to —4 per cent on Jan. 25, 1937. The thyroid gland was apparently enlarged and felt a great deal softer than on the previous admission. This decrease in consistency was thought to be due to the colloid reaccumulating rather rapidly in the gland.

Another biopsy was performed in order to determine the histologic status of the gland at this time, when the influence of oral administration of thyroid had

been discontinued. Typical sections from the gland at that time are shown in figures 6 and 7.

The most extraordinary histologic transformation had occurred after discontinuance of the feeding of thyroid by mouth. The follicles were everywhere filled with homogeneously staining colloid, and except for a few, between which the intrafollicular septums had ruptured, were slightly larger than those encountered in the normal gland. The colloid seemed fresh in appearance, and where the follicle was distended abutted on the epithelium or was prevented from doing so by an accumulation of chromophobic vacuoles. The follicles were everywhere spherical, lined with active epithelium which varied from high cuboidal to columnar. The nuclei were less pyknotic and much more nearly spherical, and in some nucleoli were evident. The cytoplasm of the cells was plentiful and took a pink stain diffusely throughout the cytoplasm, except for areas in which there seemed to be accumulations of chromophobic vacuoles and chromophilic granules. The appearance of the follicles was entirely different from that in previous sections. In some areas the epithelium was actually comparable with that which occurs in cases of hyperthyroidism, in that there were marked hypertrophy and hyperplasia and signs of pronounced cellular activity. The interfollicular material was markedly reduced, there being little except a few endothelium-lined, flattened capillaries and some relatively inconsequential amounts of white fibrous tissue, which probably represented the normal septums of the gland. The areas of dense lymphocytic infiltration with germinal centers could no longer be observed. The gland had the appearance of marked activity as a result of withdrawal of oral thyroid therapy and throwing of the gland on its own resources. The secretory mechanism seemed to be functioning efficiently and rapidly. The cellular constituents of the parenchyma were in an active physiologic state as far as one could tell from the histologic appearance. The follicles, ballooned up to their previous size, were filled to their utmost capacity with homogeneously staining colloid, which first distended and then compressed the interfollicular tissue and accumulations of cells, thus creating the appearance of a marked reduction in the stroma. A general estimation of the number of follicles per field in this section, taken four months after discontinuance of thyroid therapy, gave one the impression that no actual loss of tissue had occurred during the atrophic resting state but that the follicles were merely collapsed and shrunken because they were drained of all their colloid through gradual absorption or excretion. The threshold stimulus for the gland to secrete was never reached on account of the artificial feeding of thyroid. After this had been discontinued for four months the stimulus for the gland to secrete was again present, and this was met by marked increase in the cellular activity; thus colloid was deposited, as was shown in the final section, which represented practically a reversion to the primary stage of simple colloid goiter. Evidently this state of hypersecretion together with hypertrophy and hyperplasia of the epithelium preceded the formation of a colloid goiter, at least in this instance and in all probability in others. It thus may be that a state of secretory activity may always precede a colloid goiter, and it would seem also to be a matter of fact that when there is not sufficient threshold stimulus for the gland it will undergo atrophy followed by hypertrophy and hyperplasia when that stimulus is restored to normal.

This change in the histologic appearance of the gland was interesting and instructive, for it seemed to indicate that the thyroid was on its way back to its previous state and was going through a period of hypertrophy, hyperplasia and

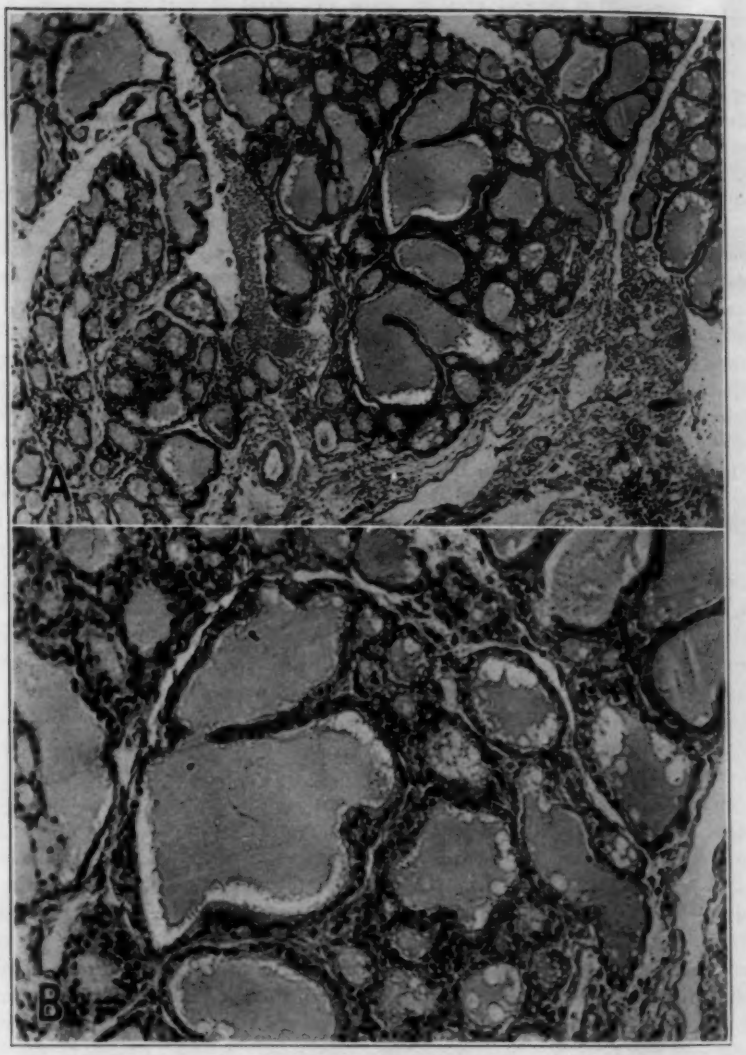

Fig. 6.—*A*, photomicrograph (hematoxylin and eosin, × 100) of tissue from the same patient after oral administration of thyroid had been discontinued for four months. The thyroid gland was enlarged, and the basal metabolic rate had fallen. The follicles were beginning to fill with colloid; the epithelial lining follicles were active and in many places were columnar. Secretory vacuoles were present. The follicular stroma was much diminished by filling of the follicles, part of the stroma having been composed of collapsed follicles giving the appearance of cords of epithelial cells. Distention of the follicles had also displaced and compressed the interfollicular septums and the blood vessels. Generally the follicles were smaller than those in figures 2 and 3, and their process of refilling was probably only partially accomplished. *B*, high power photomicrograph (hematoxylin and eosin, × 200) of the same section. Note the secretory vacuoles and the hypertrophy and hyperplasia of the epithelium.

secretory hyperactivity due to the fact that the body demanded secretion of the gland (which during the recent atrophic stage had been supplied by the oral administration of thyroid).

It is to be noted here that during this stay in the hospital the basal metabolic rate was recorded on two occasions as —15 and —4 per cent, respectively, and

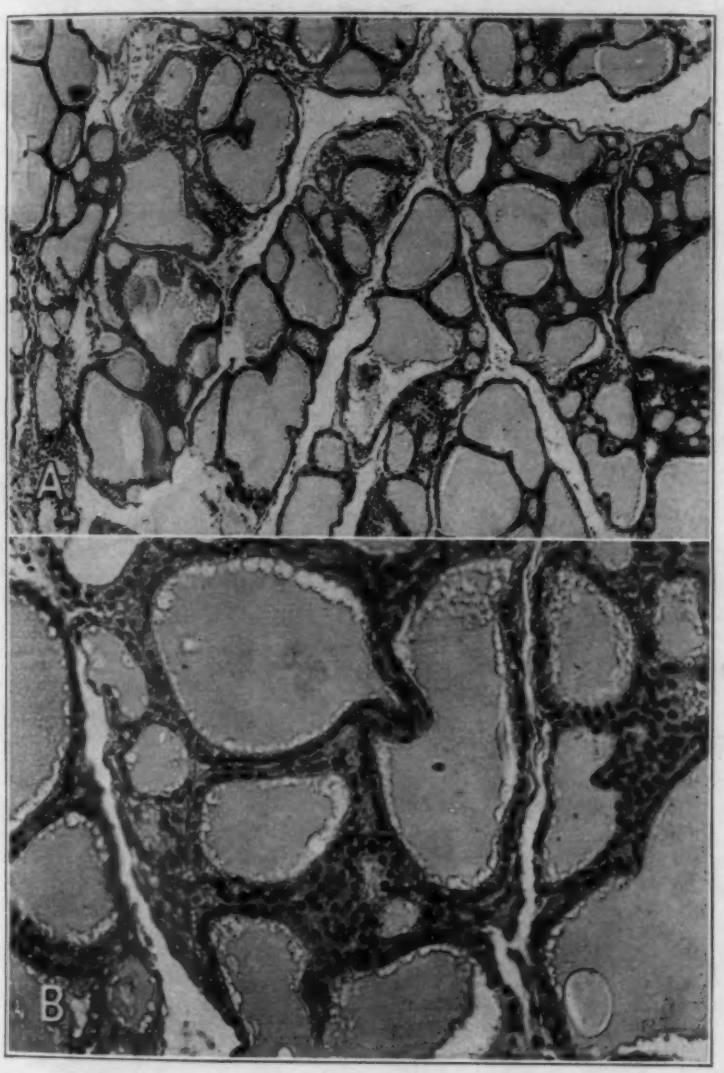

Fig. 7.—*A*, photomicrograph (hematoxylin and eosin, × 100), showing epithelial hyperactivity with the refilling of the follicles with colloid. *B*, high power photomicrograph (hematoxylin and eosin, × 200) of the same section. Note the refilling of the follicles with colloid and the epithelial hyperplasia. Figures 6 and 7 are to be compared with figures 4 and 5.

yet the histologic appearance of the thyroid was that of pronounced cellular activity, i. e., hypertrophy and hyperplasia. This suggests that in this instance, at least, colloid goiter may have been preceded by a period of histologic activity not only from the state of a normal gland but even from that of an atrophic thyroid. In order to determine this point it was decided to let the patient go without any further thyroid by mouth for another three months. This was perhaps a stage of hyperactivity on the part of the gland that precedes the stage of inactivity or lessened activity associated with increase of colloid and inability of the gland to excrete its secretion. Accordingly, the patient was discharged from the hospital, and in three months she was readmitted for a fourth biopsy. Thus, the period without thyroid by mouth was seven months. The patient had gone back into her original state of hypothyroidism. The thyroid gland, although not

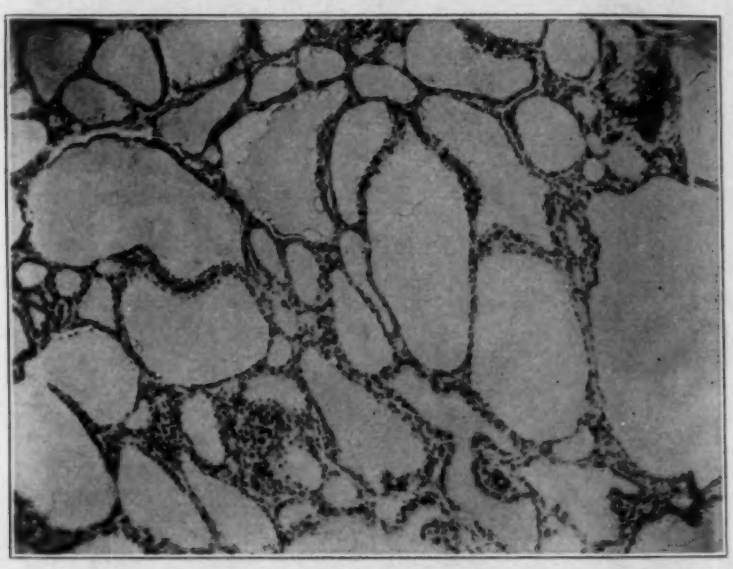

Fig. 8.—Photomicrograph (hematoxylin and eosin, × 100) of a biopsy specimen from a patient six months after oral administration of thyroid was discontinued. The follicles are larger than normal, the epithelium returning completely to the resting, inactive state. This occurred simultaneouly with the clinical signs and symptoms of hypothyroidism and redevelopment of colloid goiter.

quite as large as at first, was prominent and, except for the two small scarred areas, was essentially as soft as before. The basal metabolic rate at this time was —13 per cent. Biopsy revealed a complete revision to the previous state of histologic inactivity (fig. 8).

The patient was then discharged from the hospital and directed to take 2 grains (0.13 Gm.) of thyroid a day. She has been taking that amount since April 1937. In the interval she has remained perfectly well. Her signs of hypothyroidism have disappeared; her thyroid gland cannot be seen, and it is felt with difficulty. The 2 grains of thyroid seems to be just the right amount to overcome her natural

deficiency, and at the same time it permits sufficient atrophy of the gland to accomplish a favorable cosmetic effect and do away with the goiter.

In July 1936, in the Johns Hopkins Hospital, with the permission of Dr. Dean Lewis, Dr. Fred W. Geib, the resident surgeon, repeated for corroboration the observations described. Three biopsies were performed on a patient with diffuse colloid goiter before and during the oral administration of thyroid. The details of this case are as follows:

CASE 6.—A. W., a white boy aged 15 years, was admitted to the surgical service on May 28, 1935. The clinical diagnosis at this time was diffuse colloid goiter with hypothyroidism. At the age of 11 years this patient had noticed that his neck had begun to enlarge, and for four years the increase had been continuous. In the last year he had taken iodine pills frequently and had rubbed "iodine salve" on the skin of his neck over the goiter. During this period the increase in size of the gland had been accelerated, and it had become much harder. (This is the usual history obtained from patients taking iodine over long periods.)

Examination of the patient at this time revealed a fat boy, rather sluggish, with puffy features. There was a large, collar-like mass in the neck which on palpation was very soft. The pulse was slow, and the patient presented the clinical picture of diffuse goiter with hypothyroidism. The basal metabolic rate was —11 per cent.

Biopsy of a specimen from the thyroid at this time revealed typical diffuse colloid goiter.

In the outpatient department the patient was given 1 grain (0.06 Gm.) of thyroid each day, and by June the basal metabolic rate had risen to +15 per cent, a total of 25 points. In July 1935 the oral dose of thyroid was elevated to 1 grain (0.06 Gm.) twice a day, and by July 23 the basal metabolic rate had fallen to —2 per cent. This decrease in the basal metabolic rate occurred in spite of an increase in the amount of thyroid the patient was receiving by mouth. Simultaneously the thyroid gland had become much smaller and harder. The patient continued to take 3 grains (0.19 Gm.) of desiccated gland by mouth for ten months, at the end of which time he was readmitted for biopsy (April 4, 1936). At this time the thyroid was reduced even more in size, so much, in fact, that no sign of a goiter was present. The remaining gland was very hard and had obviously undergone pronounced atrophy. The basal metabolic rate on this admission was +4 per cent. The general condition of the patient, both physically and mentally, had vastly improved. Biopsy at this time supported the clinical impression that there was atrophy of the thyroid gland. The microscopic appearance was characteristic of the disuse atrophy observed in the previous case and shown in figures 10 to 13. The patient was again discharged from the hospital and advised to discontinue taking thyroid by mouth. He returned in four months, when a section of his thyroid gland revealed a reaccumulation of colloid such as occurred in case 1 (figs. 6 and 7).

Since that time a number of patients with large diffuse and soft nodular colloid goiters associated with a low basal metabolic rate have been successfully treated by oral administration of thyroid in increasing doses over a considerable period—a number of months. In all the goiter has been reduced, if not completely to the size of a normal thyroid, so

effectively that the patients were completely satisfied from a cosmetic standpoint. The restoration of their metabolism to within normal limits has resulted in a pronounced improvement not only in their physical appearance but in their mental reactions.

COMMENT

From the clinical as well as the microscopic standpoint, atrophy of the thyroid gland has been produced by oral administration of tablets of desiccated thyroid. The extent of the atrophy as well as the permanence depends on the size of the dose. As the thyroid of the recipient becomes more and more reduced in size and function, ever increasing doses of thyroid must be administered to maintain the same degree of hyperthyroidism. In spite of the possibility of developing antihormones, the explanation of the latter observation may well be found in the gradual diminution of secretion of the patient's own thyroid due to disuse atrophy of the gland and requiring additional amounts of thyroid by mouth. This same tendency has been noted during administration of solution of parathyroid as well as of insulin. It may be stated as a biologic law that organs whose function is no longer necessary go into a regressive state, and it would appear to be applicable to the endocrine glands. The function of such glands is in all probability regulated by the concentration of their secretion in the blood or tissues. When the glandular secretion in the blood stream is consumed, a temporary response on the part of the gland is produced, with a proportional mobilization of its secretion. A typical example is the mobilization of the hepatic sugar and the level of blood sugar. The thyroid secretion in the blood stream probably determines the degree of activity of the thyroid parenchyma at any given time. Thus the cellular activity of the thyroid gland would take place at a minimum rate in the presence of an abundance of exogenic thyroid in the blood stream. The changes observed in the histologic structure of the thyroid described here would seem to bear out such a hypothesis.

It is a conjecture, but not beyond the realm of probability, that in forms of enlargement of the thyroid other than simple colloid goiter, atrophy may be accomplished in a similar manner. It is even possible to conceive that the diffuse hypertrophy and hyperplasia associated with hyperthyroidism could be brought under control to an atrophic state, and this interesting problem is being investigated at present. In order to produce such a change in the gland a slightly larger amount of thyroid must be administered artificially than is sufficient to equal the rate of secretion of the thyroid gland. As the size of the gland diminishes and the consistency gradually increases, the amount of exogenous thyroid

may be reduced proportionately until the minimal requirements have been determined. It will probably prove necessary to produce at least a mild degree of relative hyperthyroidism in cases of the colloid type of goiter before definite atrophic change in the thyroid will be brought about. The degree will possibly vary with the patient, according to age and the size of the gland. Another variable factor will undoubtedly be the period necessary for administration of thyroid by mouth. It is to be noted, however, that in patients afflicted with nodular or diffuse colloid goiter there is a coexistent state of clinical hypothyroidism. Soon after thyroid medication is begun there is a striking improvement symptomatically, and the further development of low grade hyperthyroidism is so insidious that the patient is unaware of any unpleasant effects of the increased thyroid medication. On the same principle, thyroid in small doses, 1 to 2 grains (0.06 to 0.13 Gm.) per day, has been administered by mouth to patients recovering from operation (double partial lobectomy) for hyperthyroidism. In these cases the sudden fall of the level of thyroxin in the blood stream is broken, and at the same time the brunt of the demand which originally caused hypertrophy and hyperplasia of the gland to occur is satisfied largely, if not entirely, by the thyroid artificially supplied. The glandular tissue remaining after operation is in this manner given an opportunity to quiet down and pass into an inactive state histologically. Thyroid medication has been discontinued by gradually diminishing the dose over a period of three weeks. Further periods of administration of thyroid may be employed in the future if there is a tendency to recurrence of the hyperthyroidism or if hypothyroidism persists.

It may prove after further experience and investigation that another type of diffuse goiter with hyperthyroidism might be benefited by oral administration of thyroid, that is, the so-called "iodine-fast thyroid," in which the follicles are filled with colloid after administration of iodine but in which clinical hyperthyroidism has recurred after escape from an artificial iodine remission. Further remission cannot be obtained in this type of gland, because successive colloid tamponades cannot be induced by prolonged administration of iodine. Gradual absorption of the deposited colloid associated with atrophy or diminished function of the thyroid should, even if complete atrophy cannot be accomplished, at least permit an efficacious colloid tamponade after resumption of iodine therapy. Exogenic thyroid, by resting the hyperplastic gland, enables it to absorb the entrapped colloid. As things now stand, patients with this condition are denied proper preoperative preparation, and they afford a relatively poor surgical risk.

The fate of the colloid in the transition from a colloid goiter in which the follicles are bulging with colloid to the atrophic stage in which the acini are essentially empty and shrunken is a matter of conjecture. The epithelial cells may absorb it, or the larger part may be excreted from the follicle, after which, the demand of the body having been removed, there is temporary cessation of epithelial secretion. The small amount of colloid present seems to be inspissated. The clear cytoplasm of the epithelial cells in the atrophic stage would also suggest that, secretion having ceased, the follicle once emptied by discharging its contents had not been refilled. The depletion of colloid might suggest that active secretion of the thyroid is chemically bound to it rather than held merely by adsorption, in which latter case the colloid, acting as a mere vehicle, would remain after consumption of the secretion.

The histologic appearance of the stage of atrophy, if observed without knowledge of the microscopic appearance before and after the onset of this stage, would give the impression of a chronic inflammatory process associated with diffuse and pronounced destruction of the parenchyma of the thyroid. The apparent fibrosis; the atrophic follicles, which in many fields appear as cordons of epithelial cells without a lumen; the dense desiccated colloid, and the pronounced infiltration of the parenchyma with small lymphocytes, even forming germinal centers, in many ways corresponds with the histologic appearance of struma lymphomatosa of Hashimoto. It will be recalled that the last-mentioned condition is supposed to be a forerunner of Riedel's struma. The microscopic appearance of the thyroid in cases of cortical atrophy of the adrenal in which there is atrophy of the thyroid histologically with marked infiltration of the lymphocytes is similar to that described here.

MacCallum [4] called attention years ago to the infiltration of the struma of the thyroid gland with small lymphocytes in patients suffering with hyperthyroidism. It is thus interesting that in the patient in whom an artificial hyperthyroidism has been produced the thyroid, though atrophic, is everywhere invaded with these cells, the concentration in certain areas simulating germinal centers. After administration of thyroid by mouth has been discontinued and hyperthyroidism has subsided, biopsy reveals that the lymphocytes have disappeared entirely from the gland. It may be that the thyroid secretion has a stimulating effect on the thymus.

From the sequence of changes noted in the microscopic structure of the thyroid gland following oral administration of desiccated thyroid, it seems possible that the mechanism of secretion of the thyroid cells might continue to function even hyperactively, but the mechanism for discharge

of this secretion into the blood stream may, for unknown reasons, fail. As a result, storage of an excess amount of colloid in the follicles would occur. Secondary pressure effects, such as ballooning of the follicles and pressure on the follicular septums with flattening of the lining epithelium, would follow, resulting in the histologic appearance of simple colloid goiter.

One point would seem very likely, i. e., that two separate functions are fulfilled by the follicular epithelium, one the manufacture or secretion of thyroxin and the other the release of thyroxin into the blood. Interference with the balance of the usually smoothly functioning mechanism will produce extensive histologic changes within the gland and physiologic disturbances in the organism as a whole.

OPINIONS ON THE APPENDIX AFTER THIRTY-FOUR YEARS

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This article has been written purposely in a style that is entirely foreign to the usual scientific publication, which follows a strict cut and dried pattern, stating the problem with its history, experimental and clinical notes and discussion, then closing the article with conclusions. Probably the main reason that this discourse does not follow the usual routine is because it is believed this will be enjoyed by Dean Lewis, who in his prime, endowed with that gift of the warmest human relationship, always maintained his students' utmost interest by striving for something new, different from the ordinary and entirely free from dulness. Although this article may seem to lack the genius of Dean Lewis and contains nothing startling, it no doubt expresses the opinions of many general surgeons. Further, it may bring out many truths not to be found in much of the literature on this most common of surgical conditions. It is believed that even in the most formal medical journals an occasional publication of this type will be welcomed by the physician.

"The appendix should be removed at the earliest possible convenience."

Most surgeons become more convinced of the truth of this statement with each year of their experience and wonder why there was ever created a small, wormlike rudimentary hollow tube at the beginning of the large intestine in practically every mammalian. At times it seems its sole purpose is to cause pain, suffering and death, and at the same time to give the surgeon the opportunity to do some of his most noble work. Yet in spite of surgeons' most noble efforts and study with marked modern scientific advancements, the appendix, in the role of the most common and most prevalent major surgical problem, still brings to persons of any age a dangerous and treacherous condition. This ominous, degenerate small organ, as it has done in the past, continues to pay many a young surgeon's bills and brings him into the lap of luxury in some instances, a fact of which most surgeons are well aware; nevertheless, in most instances the surgeon's recompense, no matter how great, cannot match the service he is rendering the patient by removal of this structure.

After thirty-four years of general surgical practice, in which approximately 2,500 appendixes have been removed and during which the many statistical and scientific accounts in medical journals from various sections of the country have been appraised, medical and surgical clinics

attended and the medical and surgical fads mixed with real scientific progress observed, one cannot help acquiring a definite philosophy on the appendix, some of which has already been expressed.

Every community, from the rural settlement to the largest metropolis, is made up of persons who are all capable of having "bellyaches" and as such are all candidates for possible trouble with the appendix. Educating them to regard with concern the common "bellyache" has done much to bring these persons to the physician early. In spite of this, instinct seems to tell many that to move the bowel will relieve the pain, while others procrastinate with the ice bag and remedies "of great and low degree," and after failure of these finally see the physician. Avoidance of laxatives and of procrastination is the only salvation for the person with an angry or poorly behaved appendix. A crusade against these two factors seems to be the main point of attack to reduce the entirely too high mortality rate from disease of this degenerate organ.

Because of laxatives and procrastination, together with individual peculiarities of development and reactions as varied as people themselves, the surgeon has to be prepared for almost any type and condition of appendix when he begins his search. Most surgeons may have a good idea of what they will find and how, why, where and when they will find it before they operate, but there is not a surgeon living today, nor has there been one, no matter how great (except the Great Healer) nor is it believed there will ever be one who can foretell the findings each time before the abdomen is opened. Even after opening of the abdomen, on some occasions great surgeons have been baffled. But once the appendix is found and identified as the culprit (and even when it appears innocuous but no other criminal is identified), two problems remain, namely, what technic shall be employed in the handling of this degenerate and what after-care shall be given the rest of the body to which the appendix is doing or may do harm.

Diagnostic methods, surgical technic and treatment, including that following operation, are well taught to the present student in the approved medical school and internship. Logic explains that practically every surgeon and physician wishes to see his patients do well, and to this end he will strive to develop the best methods and technic possible. He will try to improve and adapt to his own peculiarities and best abilities that which he has learned from school, internships, clinics, journals and probably most of all, his experiences. Consequently, surgical methods and after-care and treatment, although in most instances similar, show minor differences almost as varied as the surgeons themselves, with the end results of the conscientious ones practically the same. One occasionally wonders why two surgeons in opposite corners of the continent, employing different methods and technics and having somewhat

different ideas, manage to get the same end results in their honest statistical columns, while each using the other's method would meet with disaster. Possibly this may be explained by the fact that each surgeon has learned to know his abilities, his shortcomings, what he can accomplish and dare try or do, together with the fact that he knows his community and its people and has developed his own special methods and technic.

Technic and method of dealing with the appendix in Bismarck, N. D., are presented in the following story in résumé of a thirty-four year period. Probably all over the United States surgeons have encountered identical or slightly varying experiences, the story of which might read similarly to this one.

Impressed with my training in the clinics of J. B. Murphy, A. J. Ochsner and my other instructors, I set out in surgical practice in this small western community. Still fresh in my memory and ringing in my ears were some of the words of advice and wisdom of these great surgeons—words and truths that have stuck with me and proved their worth for thirty-four years:

"Pain without fever—appendicitis. Fever without pain—typhoid."

"Sudden or acute abdominal pain—appendicitis until proved otherwise. Always give the patient the benefit of the doubt."

"There is no argument whether a patient has appendicitis or not—remove the appendix."

"Pain, nausea, tenderness, then temperature."

"There is no honor in removing a ruptured, gangrenous appendix; it should have been removed before it ruptured."

With these and many other maxims I began my surgical activities. It did not take long to find that the majority of my surgical cases, as they have continued to be, were cases of appendicitis. Much to my sorrow, a large percentage of the patients were not seen early, as they had frequently been in the Chicago clinics, but instead came in by buggy and train from points hundreds of miles away, with abdominal conditions days or weeks old. Appendical abscesses and perforated gangrenous appendixes seemed more frequent than I had ever thought they would be. Schools and teaching clinics were not located in communities where their patients had so many miles to travel and where some education of the public had taught them not to rely on home remedies for "bellyaches." I soon found myself draining many appendical abscesses. Once the abscess was drained, the patient received the Murphy drip per rectum and hypodermoclysis with standard saline solution (physiologic solution of sodium chloride was not used in Bismarck then), managing to obtain what appeared to be an adequate fluid intake otherwise than by the oral route. Plenty of morphine seemed not only

to make these patients more comfortable but to hasten their convalescence, as it has continually proved to do. Most of my patients, sometimes surprisingly even to me, although draining unbelievable amounts of foul pus, got well. I then wasted no time in explaining to them that with their recovery they should be sure to return and have the appendix removed in the near future. That was a different matter, for once a human being is feeling well the future seems to be forgotten. I waited, but many did not return as advised, and frequently those who did were forced to do so because once again they had an appendical abscess. Once again I could only drain the abscess and impress on them that this time they must return to avoid a similar experience.

Gradually I began to wonder why some of these patients with appendical abscesses could not have their appendixes removed at once, since frequently they failed to return as directed. Consequently, just before the United States entered the World War I began to remove more and more appendixes, taking the greatest care not to spread the infection or break down nature's resistive barriers. I found that my mortality rate did not increase. From that time on I removed more and more appendixes. Thus it has not been necessary for the patient to return, and the end results have been apparently as good as previously. I have read the numerous fine reports of surgeons who have decreased their mortality rates by postponing operation in certain select cases, parenteral fluids, morphine and conservative measures being used until masses in the right side have subsided. In this western community I have hesitated to do this (although occasionally there is a case in which I postpone operation), and in comparison my mortality figures seem favorable, with the advantage that the patient has the appendix removed without the risk of a later surgical procedure. My best end results are obtained by removing the offending organ when possible and as soon as possible after a diagnosis of some type of appendical disturbance has been made. It goes without saying that after traveling miles many of the patients are tired, cold and in mild shock, and for these it has been found desirable to wait, frequently as long as eight hours, until they are rested or the shock is relieved, before submitting them to operation.

In the diagnosis of appendicitis I have found that a carefully taken history and a careful physical examination are usually all that is necessary. In the early days I did not have the benefits of blood counts, differential counts and "shifts to the left," but I soon learned not always to depend on the blood count. Often the patient's history alone was worth a dozen blood counts. Helpful as laboratory procedures have been, they are not to be trusted explicitly at any time, and with them, as with other diagnostic methods, I have failed, as does every one, to make the correct diagnosis in some cases. With time it has become

apparent to me that, although one may have a good idea of what is present in the region of the appendix, one cannot be absolutely sure of the diagnosis and findings until one gets into the abdomen, and even then sometimes one fails to find the proper solution of the problem.

In my early cases in which drainage was required I found that even with the McBurney type of incision a postoperative hernia would occasionally occur. It occurred to me that if I made this incision farther over to the side there would be less abdominal pressure and consequently possibly less chance of herniation. As the appendix is usually opposite the anterior superior spine, I began making my incisions much closer to this and toward the side, usually about 1 inch (2.5 cm) from this palpable prominence. Not only did this type of incision seem to afford an easy approach and better drainage, but it did away with herniations. Through the years I have considered this type of incision the one of choice. I have found that a large incision is not necessary, but this one can be enlarged without difficulty. When I cannot accomplish through this incision all that is desired, I have always remembered that this incision can be quickly closed and a new approach made through a right rectus or a midline incision, remembering that these other types of incisions are apt to increase morbidity. Once through the skin and external fascia, the external oblique muscle is incised in the same diagonal approach. The wound is retracted toward the midline, and once again exactly opposite the anterior spine a nick is made in the aponeurosis of the internal oblique muscle. I usually tell my assistants that they should have no trouble finding this point, for the point of incision is labeled by the fibers making a V which points toward the anterior superior spine. A forceps is then placed in this incised nick, and the fibers are spread down to the peritoneum, which is picked up, and the abdominal cavity is opened. In closing the abdomen two continuous sutures in this aponeurosis are usually adequate.

During my student days it was of interest to me to note how long it took some surgeons to find the appendix. It seemed to be right under their fingers, and I often wondered why they did not just pull it out. I decided early to try to develop a definite method whereby I would not have to feel so long for the appendix, realizing that use of sight greatly aids the search. This early decision brought out the fact that by beginning opposite the anterior superior spine and guiding my fingers posteriorly along the parietal peritoneum toward the midline I usually encountered a fold of the peritoneum holding the cecum or appendix (not the mesoappendix), and by hooking my fingers under this and pulling gently upward and toward the wound I frequently brought the appendix into view. Many of my assistants have learned to use this method, and, although it is known that it does not work in every case,

it seems to be worth while in the majority of cases, so that a prolonged search is not necessary. Every new assistant I have is told of this method and is advised to look in the anatomy books for this "appendical ligament," which he usually does, returning with skepticism but soon saying, "It sure works and saves time hunting for the appendix."

It has always been necessary for me to buy my own catgut in the community and local hospitals. I soon found that with a satisfactory technic it was not necessary to use more than one tube of catgut for the whole appendectomy, silk being used for the skin. My assistants soon find that it is not necessary to use more than one tube of plain catgut. Lately I have watched some of my assistants use silk and have noted articles favoring silk over catgut, but after thirty-four years I am in no hurry to change.

For plain acute appendicitis, clamping and cauterizing with phenol neutralized with alcohol has seemed to serve me well, the stump being tied and inverted in a purse-string suture. After the purse-string suture is tied the strings are left long and placed around the mesoappendix, and it is ligated and its clamped forceps released, this being brought directly over the cecal area of the appendix. Occasionally this cannot be accomplished, and a separate tie around the mesoappendix becomes necessary, but this has worked out well in the majority of my cases. When I have had the opportunity to inspect this later it has presented a smooth area, free from any adherence to the abdominal peritoneum. For the gangrenous appendix, for the ruptured appendix and in cases in which a purse-string did not seem advisable I merely tied off the severed appendical stump. I found that occasionally fecal fistulas were occurring. To avoid this I developed a method of putting a few sutures in the severed stump of the appendix, usually above the clamped forceps, and then tying the stump below this suturing, which was also tied. After this, fecal fistulas became a rarity, but how this was accomplished and why I do not know.

The matter of drains was always of interest to me. I have carefully watched the numerous articles on drains, including their uses and abuses. I admire surgeons who get excellent results in closing abdomens that I would perhaps drain, yet I feel that my end results are comparable, with just as few adhesions and not much longer periods of hospitalization. I have noted the many articles proving that the peritoneal cavity cannot be drained and that it is foolish to try to drain it; still I like to see drains go into the abdomen when I feel it is necessary. I like to use the common Penrose rubber drain. At one time I found that occasional subphrenic or pelvic abscesses were following "purulent appendectomies." To avoid these abscesses I began putting down one drain toward the pelvis and one toward the liver, besides the third down to

the appendical stump in the "purulent cases." Since then I have used three drains in this manner. Students fresh from internships, assisting me, have wondered if I was not spreading pus by placing the drains in this manner. They found to their surprise, as I had known they would, that the patients got well without pelvic and subphrenic abscesses and when followed in after years did not seem to be troubled with adhesions.

After the war I introduced dextrose solution into Bismarck for the first time. This seemed to be of considerable benefit for patients requiring drainage, but I still dread to think of the chills that used to occur. I marvel now at the intravenous solutions available and the ease of giving adequate parenteral fluids. In fact, because of this ease I have cautioned my helpers against too much of the electrolytes.

There are many more things that could be mentioned in this story of the appendix, such as stomach tubes with modern suction bottles for distention, positions of the patient, hot abdominal packs, blood transfusions, the use of oxygen and many more factors, down to the use of modern chemotherapy.

I know that my methods and technic would perhaps not work as well for other physicians in other communities as they have for me. Likewise, I am certain that the methods of others would not work so well for me.

I have always been convinced that the important work of the surgeon is not the spectacular procedure lasting a few minutes in the operating room but the careful, tedious and painstaking preoperative and postoperative care. As a result of this conviction few of my patients with appendicitis die, and the majority go home without further trouble so far as the appendix is concerned.

Because of all this, a campaign to reduce the number of deaths from appendicitis should be directed not toward individual surgeon's methods but rather, as has been mentioned, toward education of the laity as to the danger connected with procrastination and the use of laxatives.

Medicine presents its greatest service in the field of prevention. There is no honor in seeing through convalescence a patient with typhoid fever that could have been prevented. Similarly, there is no honor in removing a ruptured or gangrenous appendix which should have been removed before it ruptured. Unfortunately, the surgeon does not have for the prevention of appendicitis anything comparable to the preventive measures available for smallpox, diphtheria or typhoid. Because of the nature of the process it is difficult to conceive of any prophylactic measure other than removal of the appendix. I do not recommend that one should go to his physician for a prophylactic appendectomy as he would go to be vaccinated, although it is entirely conceivable that at some time in the future the prophylactic removal of the appendix will

involve no greater risk or reaction than do present day vaccinations. At present the anesthetic dangers, the risks connected with any surgical procedure and the possible bad results from the surgical procedure itself do not justify wholesale routine appendectomies. It is believed that a prophylactic appendectomy is justified and decidedly to be encouraged for any person who has had symptoms of appendicitis, no matter how mild, for recurrence of appendicitis is the rule rather than the exception. No one knows when this recurrence may occur or how severe it may be, and occurrence of an attack when one is on a hunting trip or otherwise isolated from the advantages of modern surgical skill might prove fatal. This has occurred sufficiently often in the experience of every surgeon practically to justify this type of prophylaxis.

The appendix will always be with man, for it is known that a race of persons who have all had their appendixes removed will not beget a race without an appendix. The appendix, like all degenerates, seems to be ever a bad actor, and never will the surgeon dare trust its behavior.

In reviewing the problem over a period of thirty-four years I sometimes wonder whether, instead of carefully preserving and sectioning each appendix and studying it pathologically, it might have been just as well to have saved the appendix and every so often to have gone on a fishing trip and used it for bait. If the appendix turned out to be wonderful fishing bait, probably many more persons would not procrastinate and take laxatives but would see the surgeon early so that they might use it for fishing. Appendixes then might be at a premium, and a markedly lowered death rate from appendicitis would no doubt be the result, together with a healthier race, benefited by the relaxation of fishing.

OSSIFYING HEMATOMA AND ALLIED CONDITIONS

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Myositis ossificans traumatica is the most frequently used term under which several more or less similar lesions are described. This name is widely used in the literature to designate a condition, not including ordinary callus, associated with the reaction of certain tissues to trauma. The structures involved may include the bone itself, the periosteum, the muscle and its fascial sheaths or the tendinous attachment of muscle to bone. Other names are used to indicate these abnormal bony masses: exostosis, myositis ossificans circumscripta and aberrant exostosis. Another condition bears a strong relation to this group and is sometimes included with it; the occasional formation in scar of bony tissue, especially after operation on the urinary bladder and in the upper part of the abdominal wall.

Ossifying hematoma is usually included in this group also, but this term is not widely used. In this condition the periosteum is believed to be stripped up from bone, and the space between the two tissues fills with blood, which is gradually replaced by osseous material. Whether this conception is accurate or not, the actual lesion is sometimes confusing, as it may bear enough resemblance to periosteal sarcoma to give the clinician, the roentgenologist and the pathologist a great deal of anxiety.

These conditions should be sharply differentiated from the calcareous and bony deposits associated with chronic infection, from all tumors of bone and from the various bony dystrophies.

The occurrence of aberrant bony growths in voluntary muscle, whether or not in contact with the underlying bone, has been recognized and recorded in the literature since the seventeenth century. In 1860 Bullrak differentiated two types of the condition. The first was the rather rare and fatally progressive form, usually commencing in the spinal muscles. The second he described as a localized, self-limited form involving a single muscle. By the end of the century sufficient cases had been added to the literature to make it apparent that the self-limited form was more than a curiosity and that it was associated with trauma in a high percentage of cases. Since then the rapidly increasing use

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of the roentgen ray has facilitated diagnosis, and many cases have been added to the literature. The incidence is undoubtedly higher than has been reported, as many patients are practically asymptomatic and either are not brought to medical attention or are discovered incidentally after the lapse of many years.

The name myositis ossificans is a confusing one. The lesion involves primarily the fascial connective tissue, any muscular changes being secondary and degenerative. Although there is frequent observance of histologic changes due to inflammation, this is the normal reaction of the tissues to hemorrhage. Actual infection is rare in connection with this lesion, except possibly as a secondary postoperative consequence. After the osseous mass is removed it is usually impossible for the pathologist to determine whether the bony tissue was attached to bone, developed in muscle or other tissues of the body or was removed from an operative wound or a sinus tract unless portions of the surrounding structures are attached to the specimen.

There are three anatomic possibilities as regards the bone itself and the attached or adjacent muscle:

1. With the first type there is involvement of the bone without extension into the muscles. Excluding from consideration true bone tumors, the cartilaginous and bony overgrowths associated with growth and hormonal disorders and the osteodystrophies, there are found a number of lesions that cannot be differentiated from myositis ossificans histologically. The process is the same, i. e., abnormal osteogenesis. The only difference is that there is no extension into adjacent muscles. The simplest example of this type is the overenlargement of normal bony prominences often seen in the bones of the extremity in muscular, well developed persons. This falls within the limits of reasonable hypertrophy. When, however, this condition progresses to the point of functional disability or the formation of a definite mass it must be considered pathologic. "Rider's bone" is an example of this type, and the bayonet-like projections of bone into the soft tissues that have been reported from time to time belong in this classification also.

2. The second and most frequently described type of localized ossifying myositis is a combined lesion, in that it involves both the muscle and the underlying or adjacent bone. The bony mass may be firmly or only partially attached to the shaft and may extend for varying degrees into the muscle.

3. The third type is that occurring entirely in the muscle, with no demonstrable connection to bone and usually with a well defined capsule or periosteum-like covering of its own. There might also be included in this group certain of the aberrant sesamoid bones. Perhaps lesions

which are frequently described as solitary localized exostoses may be the result of processes similar to those involved in myositis ossificans.

Aberrant osteogenesis is not limited to the skeletal system and voluntary muscles. True bone formation has been described as occurring in the meninges, brain, arteries, lungs, lymph nodes, stomach, kidney, renal pelvis, ureter, bladder and skin, as well as in benign and malignant tumors and, indeed, almost anywhere in the body.

The mechanism of aberrant osteogenesis has been satisfactorily explained in two ways. The first is by overstimulation of normal osteogenic processes and necessitates the presence of normal bone or of detached fragments of periosteum or bone. This has been amply demonstrated by clinical and experimental evidence. The second mechanism is that of metaplasia of connective tissue cells into bone-forming tissue. The occurrence of metaplasia has long been recognized by pathologists and experimental workers, although its exact mechanism is obscure.

The following etiologic observations seem reasonable and well established:

1. Aberrant osseous formation is not a normal reparative process. If it were it should follow many fractures and contusions, whereas its occurrence following fracture is rare, and it does not often result from closed injuries of fascia or other tissues.

2. The most frequent single etiologic factor is trauma of the closed type, either single and severe or repeated and chronic.

3. Hereditary predisposition has been suggested. There is not yet sufficient information to give this belief any support.

4. The systemic condition of the patient has not been observed to be significant. The lesion commonly occurs in healthy, well developed persons. The values for blood calcium, phosphorus and phosphatase, when reported, have shown no deviation from the normal. There has not been demonstrated any disturbance of the acid-base balance of the blood. There has been no evidence of parathyroid or any other hormonal imbalance.

5. Most observers believe that the local reaction of the tissues involved is the important etiologic factor in all of these lesions. Just what conditions are necessary to the formation of these lesions is not understood. Extravasated blood may play a part. Certainly calcium, phosphorus and phosphatase are apt to be present.

6. It has been suggested that the presence of synovial membranes has favored the development of these lesions in some instances, especially about joints. There has been little evidence to support this view. The converse is more apt to be true.

There is no definite age incidence. Myositis ossificans, as usually described, is more apt to be seen in young, active persons, because these

are more liable to injury. The same is true of ossifying hematomas. The bony outgrowths believed to be due to excessive activity of certain muscles or tendons at their skeletal attachments should develop during the active years of life but may not be evident until later.

Certain muscles are predisposed to the development of myositis ossificans. The neighborhood of the elbow joint is a favorite site, either in the brachialis anticus muscle or lateral to or behind the joint as a late complication of backward displacement of the elbow. Two other muscle groups are predisposed, by reason, perhaps, of exposure to trauma: the quadriceps extensor and the adductors of the thigh.

The development of the chronic type of lesion is usually complete when seen. This fact is a valuable aid in differentiating these osseous masses from sarcoma. Trauma may be definite, or it may be obscure or even absent. The history is that of gradual development or the sudden noticing of a firm mass which usually is not tender or is only slightly so. If it is in a position where it causes pressure on important structures, the annoyance suffered by the patient calls it to his attention. If it is in a silent location it may be present for years before it is incidentally discovered.

The course of the acute lesion is more clearcut. After trauma a mass develops. This is clinically diagnosed as hematoma. It is somewhat doughy, and in the subsequent six days to three weeks, instead of resolving it becomes firmer and may even increase in size. This is, in turn, followed by definite ossification demonstrable by roentgen examination. Bone spicules have been seen roentgenologically as early as six days after injury, and distinct ossification is usually present at the end of six weeks. When there is no involvement of nerves or joints there are few subjective symptoms. The presence of a mass and slight tenderness to firm pressure are often the only evidences of trouble.

Growth is self limited and usually tends to become stationary after six weeks, but the mass may vary in size and consistency over a period of six months. There are some reports of gradual disappearance of the lesion without treatment. In many cases there are both clinical and roentgen diminution before the mass becomes stationary.

When an area of myositis ossificans is exposed at operation it is usually found surrounded by a semigelatinous substance which appears to be the result of muscle degeneration. Just under this tissue there is usually found a fibrous capsule that acts much as periosteum does in separating bone from surrounding structures. If the mass is subperiosteal it has no capsule of its own and is entirely beneath the displaced periosteum of the bone involved, as in exostoses or osteoma. If the mass extends into the adjacent muscle its capsule may be continuous with and is probably partly at least derived from the periosteum of the

underlying bone. Usually the periosteum and the capsule are indistinguishably fused at the junction. Cystic changes are not infrequently observed.

Histologic examination in the early stages shows organization of blood clot, hyperplasia of connective tissue and degeneration of muscle fibers (when muscle is involved). Some degree of chronic inflammation typical of tissue reaction to interstitial hemorrhage is usually observed. This is followed by the appearance of islands and spicules of osteoid tissue. Islands of cartilage are of frequent occurrence and are apt to be seen in the earlier stages. The late appearance is that of adult organized bone with marrow cavities, an organized fibrous stroma and a definite tendency of the peripheral portion of the mass to form a capsule. Simple calcification of connective tissue may also be present. Myxomatous tissue is not uncommon.

It is interesting to note that lesions removed during the course of spontaneous resolution may show definite osteoclast activity, with bone destruction and absorption. It is also interesting to note that occasionally a few of these lesions behave like normal bone in being subject to attack by further pathogenic processes. In 1 case observed by my associates and me, previously described by Cone, there was a resemblance to osteitis fibrosa cystica, with gross cysts and numerous giant cells. In a case collected from the literature and in 1 of our own cases there developed a spontaneous, apparently hematogenous suppurative process analogous to acute osteomyelitis. Four cases have been recorded in the literature of the development of osteogenic sarcoma in preexisting myositis ossificans traumatica. No records have been obtained of the subsequent involvement of these lesions by tuberculosis or syphilis, although the possibility of such involvement seems not unlikely.

In a paper read before the Western Surgical Association in December 1922, Dean Lewis reported his experience with myositis ossificans and discussed the interesting bony masses that are occasionally found in the scars of abdominal incisions. These masses are most often seen after operations on the stomach or urinary bladder. The acid gastric juices and the urine raise an interesting question. Bony infiltration of these scars is usually explained by metaplasia, but it is difficult entirely to exclude detached bits of periosteum in suprapubic cystotomies, and Lewis has called attention to the fact that a linea transversa in the rectus muscle represents the remains of a rib that at one time extended toward the midline of the abdomen. The undifferentiated mesoblastic cell of the embryo may remain quiescent into late adult life, and these cells of the mesenchyme may well explain many of the extraskeletal bone masses reported in the literature on this subject.

Phemister and Strauss showed that fascial transplants placed in the stomach, urinary bladder and ureters became infiltrated with bone. It

is known that normal osteogenesis necessitates a relatively high concentration of ionizable calcium and phosphorus in the blood serum and that phosphatase is involved in some way in the process. In addition, there must be a relative alkalinity of the acid-base balance of the ossifying tissue for the calcium to be deposited as calcium carbonate and tricalcium phosphate. It seems not unlikely that a local setup of the mechanism in the tissues following injury or insult might result in ossification.

Ossifying hematoma or subperiosteal blood clot with osteogenesis has been reported by a number of observers. Baetjer and Waters, in "Injuries and Diseases of the Bones and Joints," described the condition. Stone reported 6 cases in 1926, and his findings were definite.

> In each of the foregoing there was a hard blow and then a hematoma which decreased in size and later ossified. They were all under the periosteum. This would make it appear that following the injury there was bleeding next to the bone. The periosteum was pushed up and gradually stretched into various shapes, in which position ossification took place. Each tumor was bone entirely covered by periosteum. Muscle was attached to the outside, but not once was it found inside the mass. This should be proof that it is not an ossifying myositis.

Bullitt reported a case in 1927; Chiari reported a case in 1917, and Riddle and Wilson, of Plymouth, England, described such a lesion in 1926.

In a considerable series of cases of the allied conditions just described there have been 2 that caused my associates and me a great deal of uncertainty as to diagnosis and anxiety as to proper treatment. Both are now believed to have been cases of ossifying hematoma developing in close relation with stripped-up periosteum following trauma, and in both the question of diagnosis was the important factor, because both patients were sent to us with a diagnosis of sarcoma already tentatively made.

REPORT OF CASES

Case 1.—An 18 year old girl, while riding, was thrust against a projecting staple in a post by the shying of her horse. A somewhat tender area developed in the region of the left deltoid muscle. The pain subsided, but the mass continued to grow. At the end of about three months roentgen examination was made in her home city, and the condition was diagnosed as osteogenic sarcoma of the upper end of the humerus. Amputation of the arm was advised. She was brought to us for consultation by her parents, together with the roentgenograms. The mass was the size of an orange and clinically looked like osteosarcoma. The history of trauma, however, made us hopeful that the lesion might be an ossifying hematoma, but there was a history of steady growth and considerable pain. The roentgenograms were not conclusive, however, although the bony mass was mottled, and there was a faint cortical shadow indicating some walling off of the tumor from the soft parts. There was no evidence of metastasis to the chest. Dr. Henry J. Walton, the roentgenologist, leaned toward the diagnosis of a benign outgrowth, rather than osteosarcoma. The patient therefore returned to her home, and her

local surgeon removed the growth and sent it to us for study. There was considerable difference of opinion as to the nature of the mass, and it was seen by a number of pathologists. Dr. Hugh R. Spencer and the late Dr. S. M. Cone made an especially careful study of it, and the final diagnosis was benign bony reaction to trauma with subperiosteal hemorrhage. The wound healed promptly, and the patient has had no further trouble, although more than ten years have elapsed since then.

Case 2.—A girl 15 years old, one year prior to admission to the hospital, sustained several hard falls within a short time. Rather severe pain and soreness subsequently developed in the posterior portion of her right thigh. She limped, because the pain became worse on walking. She was kept in bed for four weeks; she improved but continued to have a dull ache in her thigh. She became active and remained so until six weeks before she was seen by us.

During this six week period the thigh became swollen and firm, with some stinging, burning pain. Roentgen examination made at home showed a fusiform swelling in the position of the biceps femoris muscle, and within this shadow there were a number of small, irregular islands of bonelike tissue, one of which was about 2 cm. in length. No irregularity in the femur was seen. Some irregularity of the lower margin of the ischium could be detected in the roentgenogram. The impression at that time was that of either sarcoma of the thigh or myositis ossificans.

Dr. John E. Legge, of Baltimore, was consulted, and he referred the patient to us for study, diagnosis and treatment. She was cheerful and cooperative and appeared to be in excellent general condition, her only complaint being the sore, enlarged right thigh, which was a little more than 2 inches (5 cm.) larger than the left. It was firm over the posterior half, and this firmness was more marked in the upper half. Roentgen examination by Dr. Henry J. Walton showed no change in the femur and some increase in the density of the soft tissues of the posterior part of the thigh, with several shadows of bonelike density varying from 1 mm. to 2 cm. in length in the region of the biceps femoris muscle. Dr. Walton's impression was that of myositis ossificans, and the patient went back home, to return in six weeks. There was no fever or tenderness; the blood count was normal, and the calcium and phosphorus content of the serum was not disturbed. On September 30, the findings were about the same, and the patient again returned to her home.

Soon after this the thigh began to swell and became painful, and there developed an inflamed, tender area in the subcutaneous tissues, its posterior aspect about midway between the lower end of the femur and the trochanter major muscle. Hot moist dressings were applied, and a small, superficial ulcer developed over the indurated area. There was no discharge of pus, however. At this time the patient returned to the hospital, and we were anxious lest we had been overlooking a sarcoma of the thigh.

At operation the indurated ulcer was excised and a frozen section was made, which was reported as showing inflammation, with no evidence of malignancy. The deeper portion of the thigh was explored, and a long, tubular cavity was found, containing a number of detached pieces of bone, one of which was about 2 cm. in length and looked like a small sequestrum. The tract was partially filled with a long, narrow sausage-shaped mass which proved to be a coagulum, and this tract extended up in the thigh to the level of the tuberosity of the ischium. The culture showed both hemolytic and nonhemolytic staphylococci.

A roentgenogram taken several days later showed no evidence of the small bony masses seen in the earlier roentgenograms. Because the patient had an area of roughening along the lower margin of the ischial tuberosity and because of the injury and the roentgen and operative findings, it seems reasonable to conclude that in this instance we were dealing with an ossifying hematoma, which probably became infected after the ulcer developed.

SUMMARY AND CONCLUSIONS

A confusing and varied collection of abnormal bony masses is briefly discussed.

Two cases of a condition believed to be ossifying hematoma are reported.

It is suggested that this group of lesions might be more simply classified as abnormal osteogenesis and further divided into periosteal, parosteal and extraskeletal, depending on the relation to bone and periosteum.

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SURGICAL PROBLEMS IN THE TREATMENT OF CHRONIC ULCERATIVE COLITIS

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Those who have had the unwelcome duty of caring for any considerable number of patients with chronic ulcerative colitis of the so-called idiopathic form realize that the condition presents many problems. In spite of much conscientious work and many ingenious theories, its cause still eludes discovery. The medical care of these patients is by no means acceptably standardized. Relation to other disorders and to complications is obscure. The prognosis is very uncertain. The clinical course is full of surprises and disappointments. Recurrence after years of apparent cure is well known, and sudden exacerbation of long-standing, mild forms may take place.

It is not with such phases, however, or with the handling of the surgical complications, such as perirectal abscess, fistula or stricture, that this paper is concerned, but rather with the proper place of surgical measures in the treatment of the disease itself. There is wide difference of opinion as to this place. It would seem that there is a large group of physicians who either are unaware of or disbelieve in the utilization of operative treatment for ulcerative colitis. On the other hand, many of the leading medical authorities on the condition fully accept the need for surgical intervention at certain times and in certain conditions but have no unanimity as to what these times and conditions are. The same situation exists among surgeons. In various publications from the Mayo Clinic the impression is given that surgical intervention is a bad last resort. By other clinics and other surgeons the earlier employment of operative treatment is advocated. The present paper aims to discuss this problem and perhaps to introduce clearer criteria for decisions about the part to be played by surgical measures in the treatment of ulcerative colitis.

One must first understand what surgical attack can hope to do. After a period in which appendectomy and cecostomy were employed to permit irrigation of the diseased colon from above downward, the failure of this idea has been generally admitted by surgeons experienced in this field. These operations have been abandoned in favor of complete transverse ileostomy a short distance above the ileocecal valve. The principle employed in this method has nothing to do with irrigation of

the colon from above but is designed to put the large bowel completely out of function and give it physiologic rest. This is the principle employed in the treatment of tuberculous disease of the spine and of the hip by the use of immobilization. It is the principle of collapse of the lung for pulmonary disease. It goes back to the epochal work of Hilton on "Rest and Pain." The inflamed and damaged colon no longer has to transport the ingested food. Its peristalsis is greatly reduced, and distention and mechanical irritation are lessened. These changes favor the healing and reparative forces. This is sound theory, and ample experience of many surgeons and physicians has shown that the theory often works.

The theory, however, does not always work. The clinical course of a patient after ileostomy may follow one of three directions. The colon may heal completely, permitting safe closure of the ileostomy opening and restoration of the large bowel to its normal function. Unfortunately, in few cases does the condition behave in this desirable manner. More will be said about this fact later; indeed, the purpose of this paper is to increase the number of cases falling in the group, in which this occurs. The second course taken after ileostomy may result in great improvement in the patient's general condition, but with persistent evidence of the disease in the large bowel. This is the situation that led the late Daniel F. Jones to say that ileostomy cures the patient but not the disease. There is often a surprising gain in weight, strength, blood cells and general well-being, but there persists a more or less frequent discharge of blood, pus and mucus from the rectum. The proctoscope shows persisting evidence of inflammation in the rectum and in the lower part of the sigmoid flexure. The barium sulfate enema shows a rigid colon with loss of haustration. It is obviously unsafe to reestablish the alimentary tract by closure of the stoma, as a rapid recurrence of active trouble is to be expected. The process is arrested but not cured. In the great majority of patients subjected to ileostomy this course is followed. It is an unsatisfactory situation. Their lives may have been saved, but at the price of a permanent ileostomy opening. A third outcome may follow ileostomy. The progress of the disease may not be arrested. Progressive fever, bleeding, loss of weight and anemia may occur. The pathologic changes in the colon may lead to a diffuse polypoid condition of the mucosa, and in some such cases malignant disease may develop. To save the patient the heroic measure of colectomy must often be invoked. This last course of events, like the first, occurs in a smaller number of cases than does the second (arrest of the process without cure).

The obvious problem for the surgeon is to find a way of greatly increasing the first, or completely successful, type of result. To approach a solution, one may ask the question: Why do some lesions heal com-

pletely after ileostomy? In the present state of ignorance as to the real cause and nature of the disease it would certainly be presumptuous to venture a complete answer, but it is at least reasonable to suppose that one factor in the situation is the employment of the principle of rest for the colon before that organ has suffered irreversible pathologic changes. One such change is the extension of the inflammatory process from the mucosa into the other coats of the bowel wall, with deposition of scar tissue and conversion of the thin-walled, flexible, contractile intestine into a stiff, thickened and shortened pipe. There is at least some information obtainable as to when this change has taken place. The barium roentgen study of the colon will indicate beginning loss of haustration, stiffening and shortening. It is one of the cardinal purposes of this paper to urge that ileostomy be employed *before* such alterations are detectable, or at least that the earliest indications of them in roentgen studies be considered sufficient warrant for operation. There is surely reason to think that such a criterion would notably increase the percentage of cases in which the patient is "cured" by operation.

Why does one need to set up a guidepost for operation? If early operation offers so much possibility of improved results, why are not all patients operated on early in the disease? The answers are not difficult to find. In the first place, the unpredictable course of the disease causes reluctance to resort to radical measures prematurely. In a great many cases, even in some of those in which the onset is violent, the condition abates and apparently clears up under less radical forms of treatment. It is natural to hope in each instance that this may take place and to defer surgical attack from time to time in this hope. For this reason frequent study of the roentgen appearance of the colon may prove a useful and practical guide to the onset of changes that no longer brook delay. A second and potent reason for hesitation to resort to ileostomy is the nature of that treatment itself. When an artificial anus is made through the abdominal wall, there results the need to care for fecal discharges, the trouble of providing and wearing dressings or apparatus of some sort and the disagreeable odor or fear of odor, which is most distressing to sensitive patients. When the fecal fistula opens from the ileum there is, in addition, often much difficulty in keeping the abdominal skin about the stoma in good condition. In many such cases a widespread excoriation of the skin develops in spite of all efforts to prevent it, and this is extremely painful. At times a considerable prolapse of the ileum may occur, with protrusion of a long piece of intestine, that adds to the discomfort and difficulty of caring for the ileostomy. This may require a secondary operation to correct it. One need not elaborate further to prove that treatment by ileostomy carries with it many disadvantages; indeed, as some have expressed it, the treatment may be as bad as the disease. There can be no doubt that this aspect

of the matter has had great deterrent influence both with patients and physicians against the early employment of ileostomy. A third objection is the probability that, once made, the ileostomy opening may have to be retained permanently because of failure of the colon to heal. These, then, are the very powerful influences against early resort to ileostomy. Yet, in my experience, later successful closure is obtained only when early ileostomy has been employed. It would seem proper to urge the surgeon and the patient not to trust too much in a turn for the better, to look frequently for beginning evidence of roentgen changes and to adopt the plan of treatment by ileostomy at the first sign of such changes.

This doctrine would be more readily accepted if surgeons could devise some type of operation to reduce the distressing features of ileostomy. A step in this direction has been made by Cattell, of the Lahey Clinic, who draws out the stump of the ileum several centimeters beyond the level of the abdominal skin and fixes it there. This projecting ileal stump can be inserted into the rubber bag which is worn during the day and thus permits the collection of fecal discharges with less soiling and irritation of the skin. I have employed another device in 1 or 2 cases that may prove helpful also. A young man was seen a year or two ago, whose ileostomy opening, created elsewhere, gave great trouble because of intussusception of the bowel above the stoma through that opening. There frequently resulted protrusion of a segment of intestine 20 to 30 cm. long, which soon became edematous, purplish and greatly swollen, with consequent difficulty in reducing the prolapse. Relief for this condition was sought, and in attempting it a method was devised that not only corrected the prolapse but in considerable measure altered the character of fecal drainage. There was more absorption of fluid, with a less liquid stool and less frequent evacuations.

In brief, the abdomen was reopened, and the ileum just above the stoma, which had not been disturbed, was drawn into a U-shaped loop immediately proximal to the stoma. Each arm of this loop was about 20 cm. long. The two arms were sutured to each other, and then a wide lateral anastomosis was made, running the whole length of the adjacent arms (see accompanying sketches). The ileum was then replaced in the abdomen and the wound closed. Two results were sought by this procedure. First, the bulky, self-anastomosed loop just above the stoma effectively stopped the prolapse. Second, this loop with its anastomosis formed a reservoir and peristalsis-checking trap for intestinal contents, which it was hoped would slow down discharges and aid in absorption of fluid. The latter effect was attained in part at least, the patient reporting definite improvement in this respect. Barely a beginning has been made with this method, and certainly no conclusions are possible as to its value. Perhaps combined with Cattell's

projecting stump it would be more effective. The purpose in mentioning it here is to raise the problem of operative means of delaying peristalsis and promoting absorption in the ileum above the ileostomy and to stimulate surgeons in the solution of this problem.

There is another issue of great practical importance in the handling of patients after ileostomy—to determine when the stoma may be closed with reasonable safety. This cannot be based on the general improvement of the patient. It is not uncommon to see remarkable gains in weight, with restoration of the blood to normal and absence of fever or any abdominal symptoms but with persistent ulcers in the "defunctionated" colon. Proctoscopic examination, of course, gives direct evidence of the condition of that part of the bowel that can be inspected, and until this area has returned to normal appearance there can be no

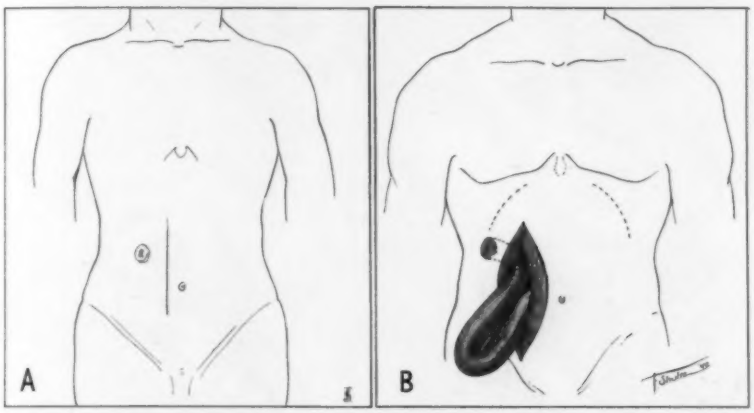

Fig. 1.—*A*, right rectus incision mesial to the ileostomy; *B*, loop of ileum just above the ileostomy, drawn out through the incision.

thought of closure of the stoma. For the higher portions of the colon, roentgen enema studies are helpful in indicating the return of flexibility and distensibility to the wall of the bowel. Another test, seemingly not widely known, has proved of much value. When the colon apparently is approaching normal, 1 liter of physiologic solution of sodium chloride is introduced into the rectum and, when expelled, is centrifuged. The sediment thrown down is examined microscopically. If a considerable number of red corpuscles and leukocytes are found, it is evident that an active inflammatory process persists in the bowel. When these finally disappear, one may safely assume that the time has come to close the stoma. In my rather limited experience this has proved a reliable guide to safety of closure.

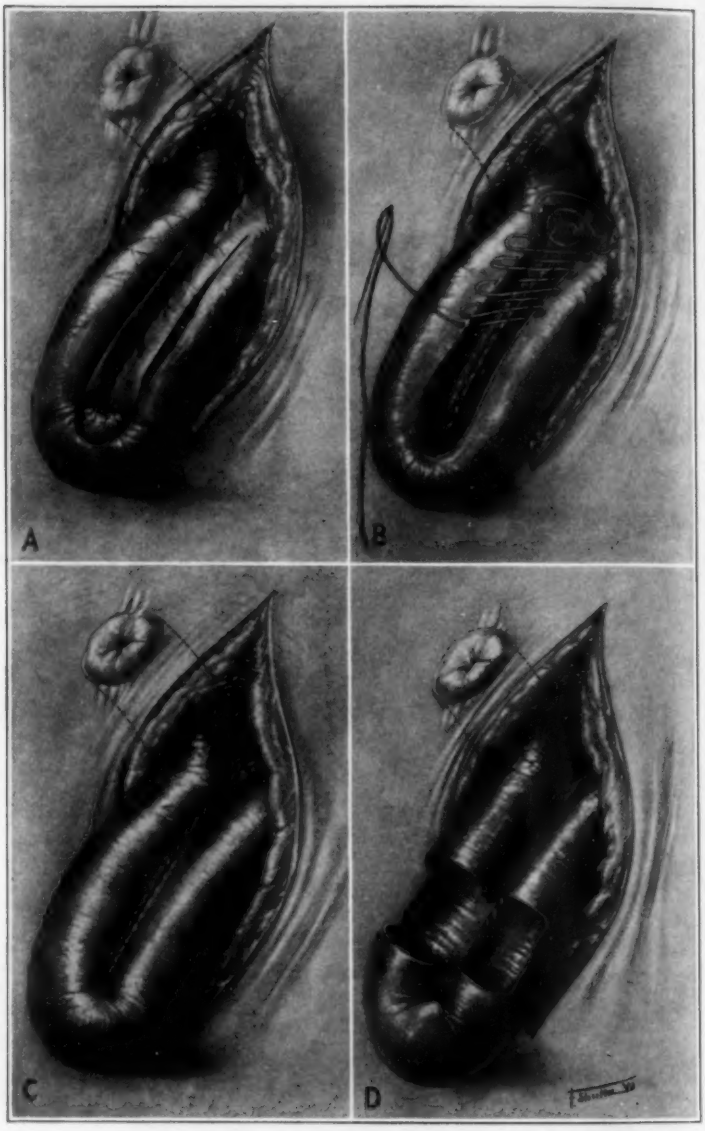

Fig. 2.—*A*, the two arms of the loop are sutured to each other with a continuous silk suture, and a U-shaped incision is begun in the adjacent arms of the loop. *B*, anastomosis between the two arms of the loop. The second row of sutures at the back, consisting of a continuous catgut stitch, has been completed, and this stitch is continued as a suture beween the two anterior edges of the incision. *C*, second row of anterior continuous silk suture. The anastomosis is completed. *D*, diagrammatic sketch with removal of a window in the anterior wall of the loop to show the side to side anastomosis.

Another group of surgical problems is raised by those patients who fail to improve after ileostomy and whose lives perhaps can be saved only by total or subtotal colectomy. These problems concern the indications for colectomy, the preparation of the patient and the execution of the resection in stages. Since these questions have already been adequately considered by others and I have no particular addition to make to this phase of the general subject, comment will be limited to calling attention to their great practical importance in treatment of the most serious type of chronic ulcerative colitis.

SUMMARY AND CONCLUSIONS

Ileostomy before permanent damage to the colon takes place is the best chance of securing a return to normal conditions, and roentgen studies of the colon are a guide to the time when it should be employed.

Improvement in the type of operation should be sought to render ileostomy a more acceptable form of treatment.

Methods of determining when the stoma may be closed with safety are described.

LUDWIG'S ANGINA

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Isadore Auguste Marie Francois Xavier Comte, a French philosopher who lived from 1789 to 1857, originated the dictum: "You can know little of any idea until you know the history of that idea."

Perhaps all physicians have speculated to themselves as to what concept or idea has fixed the name of Wilhelm Friedrich von Ludwig (1790-1865) to a pathologic condition so firmly that the attachment has existed for over a century in spite of the natural opposition of the members of the medical profession to the association of proper names with symptoms, signs or diseases.

In fact, this hostile attitude toward retention of von Ludwig's name in association with the morbid changes he described became so acute that in 1892 a heated debate on the subject took place between Délorme and Nélaton.

Even in the United States, Ashhurst, as an invited guest of the Western Surgical Association in 1929, remarked when discussing Ludwig's angina before that society that there were two schools of thought as regards the classification of diseases: One group followed the teaching of Hippocrates in objecting to the unnecessary multiplication of names of diseases and preferred to assign the so-called new diseases to their proper place under already recognized pathologic processes. The other school of thought—the Cridians (of whom I never heard until I read Ashhurst's address)—considered every new symptom and every new complication to constitute a new disease.

It is not necessary for one who knew Dr. Astley Paston Cooper Ashhurst to state that he advocated the principles of Hippocrates in this respect and did so with all the vigor and convictions of a most capable surgical philosopher.

It is interesting to recall that Ludwig's angle, the angle situated between the manubrium and the gladiolus, derived its name from Daniel Ludwig (1625-1680), a German anatomist. Furthermore, Ludwig's ganglion, a ganglion connected with the cardiac plexus and situated near the right auricle of the heart, obtained its name from still a different Ludwig, namely, Karl Friedrich Wilhelm Ludwig, a German physiologist (1816-1895). However, Karl Friedrich Wilhelm Ludwig's name is not attached to any of the many recording instruments which he introduced into physiology.

In the year 1836 a great tragedy befell the German kingdom of Wurttemberg. The beloved Queen Catherine died, and her death was due to a condition concerning which the physicians of that time had little knowledge. The affliction which caused her death was described as a "sublingual phlegmon." It is interesting to recall that when Queen Catherine died there was no dental school in Germany. In fact, her death occurred four years before the founding by Dr. Chapin A. Harris and Dr. Horace H. Hayden of the Baltimore College of Dental Surgery in 1840, which is accredited with being the first school of dentistry in the world.

I am unable to ascertain whether Queen Catherine's illness followed the extraction of a lower molar tooth, but if it did, I feel confident that she displayed Spartan courage, as strength and brute force were the only dental requirements in vogue in that period.

Shortly after the death of this popular queen, Prof. Wilhelm Friedrich von Ludwig, vice director and *Leibarzt* of the Stuttgart Hospital, at the age of 20 years addressed a medical meeting then in session in that city. He selected as the subject of his address the condition from which the beloved monarch had so recently died. About a year after this address, Camerer designated the pathologic process from which Queen Catherine died as Ludwig's angina, and as such it has been known for over one century.

Perhaps it would be both interesting and instructive to review the criteria expounded over a century ago by von Ludwig and by such a study to estimate how much the tragedy of Queen Catherine's death had to do with the continued association of von Ludwig's name with the pathologic process which caused the death of such a popular ruler.

Von Ludwig considered that the following conditions should be present in order to establish the diagnosis of the condition to which his name had been attached for so many years:

1. There should be inflammation of the deep cellular tissues under the tongue.

2. The inflammation should begin around the submaxillary salivary gland.

3. The inflammation should subsequently invade the neck and the floor of the mouth.

4. The condition should run a course which grows progressively worse, with death in ten to twelve days or gradual recovery.

Dr. John Burke, of the Buffalo City Hospital, presented an excellent translation of "Angina ludovici," together with a biography." [1]

I think most physicians will agree that these requirements are sufficiently indefinite to explain the great discrepancy of the mortality statistics published in reports of deaths from Ludwig's angina.

1. Burke, J.: Angina ludovici: Translation, Together with a Biography of Wilhelm Friedrich von Ludwig, Bull. Hist. Med. **7**:1115-1126 (Nov.) 1939.

Certainly a study of the various operative procedures and methods of treatment does not disclose a sufficient difference in surgical methods to explain the great variation in the relative number of deaths reported by the various authors, the highest mortality percentage being 75 and the lowest only 5.

This being the situation, it is reasonable to assume that there exists today a marked difference of opinion as to what actually constitutes Ludwig's angina.

Fig. 1.—Wilhelm Friedrich von Ludwig. Presented by Dr. Fordyce B. St. John, of New York.

However, I believe that most surgeons of the present time agree with those essayists whose mortality statistics vary from 30 to 75 per cent. These surgeons include among cases of Ludwig's angina only those in which the patient is desperately ill, sometimes fighting so hard for breath that an emergency tracheotomy is indicated even before any attempt is made to release the tension in the neck.

While the condition is usually a rapid process, it is also progressive, with different symptoms and signs at different stages of its progression.

Therefore, the treatment of this disease is necessarily like that of many other surgical conditions in that a careful, separate study of each individual patient is required.

A recent review of reported cases revealed that when the etiologic factor was indicated the condition followed extraction of the lower molars or the posterior bicuspids in 82 per cent of such cases. In the remaining cases such etiologic factors as calculus in the submaxillary duct, infection of the sublingual and submaxillary glands, injury to the floor of the mouth by pieces of foreign bodies being held in the mouth and infected fractures of the lower mandible were found.

Numerous studies of the various bacteria found in the cellular tissue under the tongue after incision discloses many different types of organisms, and to a large extent bacteria of the same type are also found in tooth pockets both before and after the extraction of teeth. In this group of organisms are to be found many different types of streptococci, spirochetes and the fusiform bacilli of Vincent and Plaut.

To mention streptococci at present almost automatically brings to mind the possibility of the employment of sulfanilamide or one of its derivatives both in prophylaxis and in treatment of this type of infection.

The extraction of a lower molar tooth is not, as a rule, a major dental problem, but any operative procedure done in an infected field means that there is a chance of extension of the infection unless the general system of the patient creates a sufficient defense to limit the invasion. Sulfanilamide can be given by mouth, under the skin, by rectum or intravenously in quantities to produce a concentration of the drug in the blood stream sufficient to prevent the growth of the streptococcus and often to kill this organism even after the infection has extended beyond the jaw.

If the gums or teeth to be extracted are badly involved in an infection, it may be a wise precaution to develop in the patient a concentration of sulfanilamide in the blood adequate to prevent further spread of the infection. This should be done only with the cooperation of a well equipped clinical laboratory. Sulfanilamide is not without its dangers when administered without the tests, both clinical and laboratory, so necessary for safety. To produce the desired results in such a patient would require several days at the least. However, as a rule the condition of the patient who is to have a lower molar tooth extracted is such that delay of this extent would not be dangerous and might add considerable safety to the extraction of the tooth. It is considered by those familiar with sulfanilamide that the drug has a distinct place in the field of prophylaxis in the extraction of teeth in infected fields.

The natural question that now arises is: What is the field of application of the drug when the infection has clinically extended beyond the primary infected field? The drug might be of definite aid under such conditions, but such treatment carries with it one very dangerous

possibility, namely, postponement of operative relief of tension and of extension of the infection while one is watching for the favorable effects of the drug. Certainly under these circumstances sufficient time cannot be taken even to test for or to attempt to establish proper levels of sulfanilamide in the blood.

I feel sure, from my experience in other fields of infection, that the administration of sulfanilamide or of one of its derivatives after the

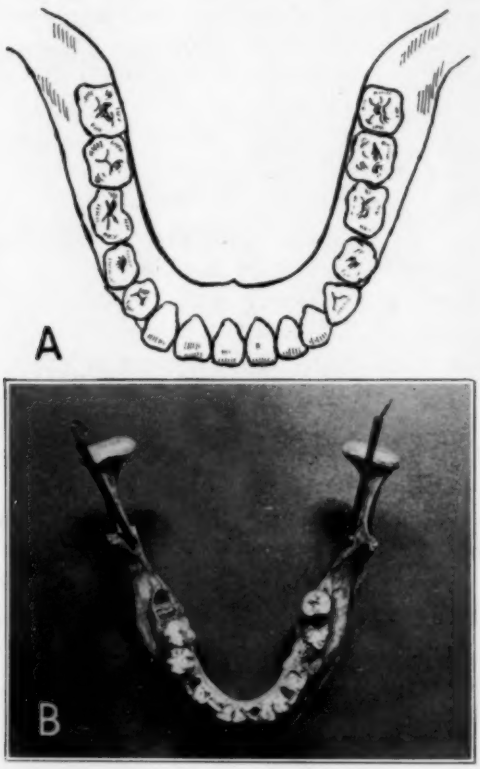

Fig. 2.—*A*, diagram showing the molar tooth "off center" and toward the midline and the anterior teeth "off center" and toward the outer side. *B*, photograph of the lower mandible, showing the same relation diagrammatically presented in *A*.

relief of tension and the establishment of proper drainage of the infected field will prove to be of considerable aid in postoperative recovery provided the drug is administered with proper care and control. It has been demonstrated that from 12 to 15 mg. of sulfanilamide to 100 cc. of blood is necessary for the maximum benefit. Such a concentration cannot be obtained quickly if the patient is allowed to consume his usual quantity of fluid; therefore, in order to bring up the blood concentration of sulfanilamide rapidly to the desired level, the fluid intake of the patient is limited to 3000 cc. or less for twenty-four hours.

Sulfanilamide employed as a fine powder has been found of advantage when placed in the tooth pocket after extractions.

Sometimes there is an ulcer found over an unerupted molar tooth and under the gum when the mucous membrane is incised in order to extract the tooth. Frequently anaerobic bacteria are associated with such ulcers. In such instances zinc peroxide as advocated by Meleney has been found valuable.

The employment of roentgen rays as an aid in the treatment of infections in the sublingual and submaxillary spaces carries with it the usual dangers associated with delay in the handling of any treacherous and rapidly progressing disease which requires immediate surgical relief of tension to prevent fatal strangulation.

In addition to the usual dangers, there is the added probability that after irradiation there will be an increase of tension due to the physiologic reaction stimulated by the roentgen rays.

As one reviews, even by a brief method, a study of the anatomy of the lower jaw and neck there stand out two very important anatomic considerations in relation to infections in this region. The first of these considerations is the fact that the tooth sockets are not in the midline of the lower mandible but are "off center." The molar sockets are closer to the inner than to the outer side. This, of course, means that there is a very much thinner partition of bone separating the socket cavity of the molar teeth on the inner side than on the outer side.

In addition to this anatomic fact, it is important to recall that the molar teeth are separated from the underlying fossa of the lower mandible only by a relatively thin partition of bone (fig. 3).

In the existence of these anatomic differences is to be found the explanation of the fact that infections are more frequent on the inner than on the outer side. Naturally, the reverse of this situation exists regarding the front teeth.

Of course, the clinical application of these anatomic observations is to be found in the fact that one can reasonably expect that any infection following extraction of the front teeth will either soon show superficial fluctuation or gradually subside. Infections following such extractions can be watched without endangering the patient's life, but this is not the case with infection following extraction of the molars, for infections of this type tend to be deep and hidden under the tongue.

The other anatomic consideration of great importance is the fact that the mylohyoid muscle is hung like a broad hammock from the lower mandible to the hyoid bone. Superficial to this muscle and reenforcing it is to be found the deep cervical fascia of the neck. These two structures (the mylohyoid muscle and the deep cervical fascia) therefore tend to confine infections following extractions of lower molars to the deep tissues under the tongue (fig. 4).

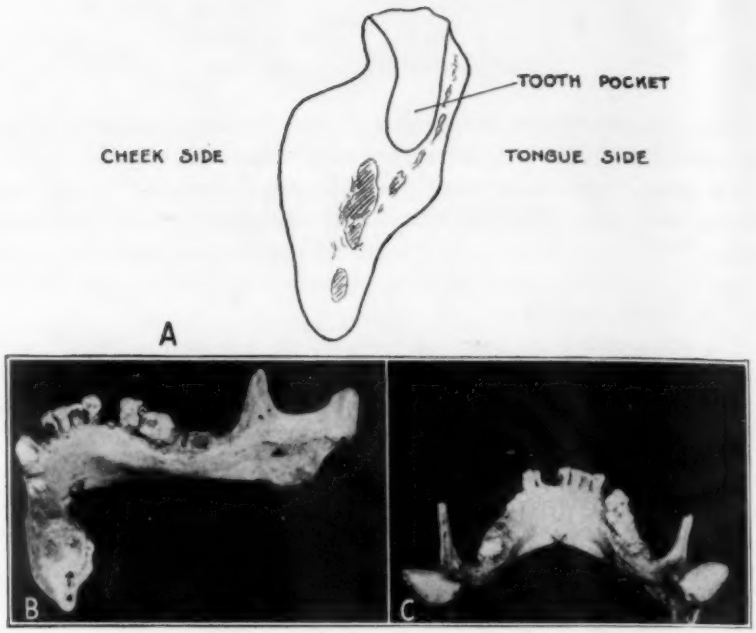

Fig. 3.—*A*, diagram of transverse section through the second molar indicating how much closer the lower part of the tooth pocket is to the tongue than to the cheek. *B*, section of the lower mandible through the second molar tooth, showing the relation diagrammatically presented in *A*. *C*, photograph emphasizing how the posterior portion of the lower mandible hangs like a shelf over the floor of the mouth.

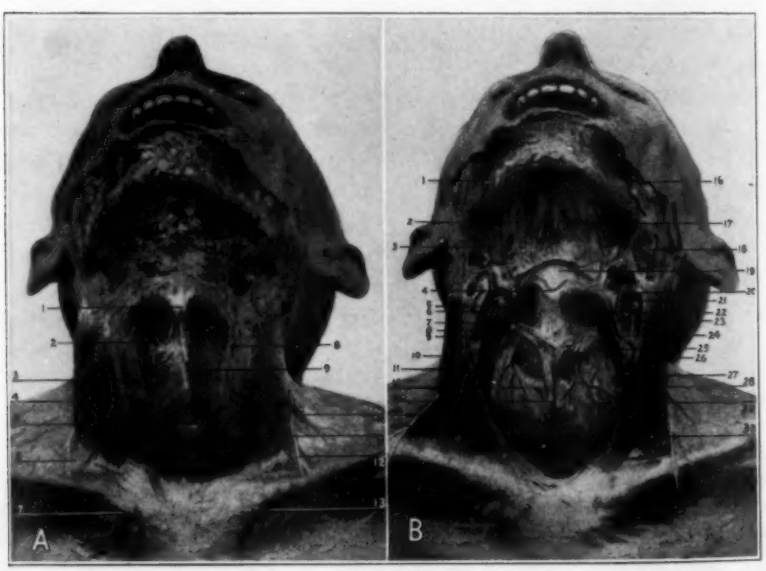

Fig. 4.—*A*, the superficial fascia. *B*, the mylohyoid muscle. The drawing demonstrates the attachment of this muscle to the hyoid bone. It also indicates the necessity of cutting the muscles transversely in order to release pressure on the hyoid bone. (From McClellan, G.: Regional Anatomy in Its Relation to Medicine and Surgery, Philadelphia, J. B. Lippincott Co., 1892, vol. 2, plates 23 and 24.)

Infections confined to the sublingual and submaxillary spaces under the tongue are the type usually included under the term of Ludwig's angina. It is this type of infection which in my opinion requires the combined vigilant attention of both the dentist and the physician. To be more definite, it is my deliberate opinion that if after extraction of a lower molar tooth a hard swelling occurs under the tongue it is the duty of the dentist to call into consultation the surgeon who may have to open up the neck widely and hurriedly in order to save the patient's life. I know of no more difficult decision than the selection of the proper time to operate for these infections. As a rule, there is no fluctuation to be felt in the mouth—in fact, very little pus is found at the time of operation. In the place of pus there is usually a large quantity of gangrenous material and other debris, such as is often found in other parts of the body where the tissues have been strangulated and the blood supply impaired.

As this swelling increases, the base of the tongue is pushed upward and backward toward the posterior part of the pharynx to such a degree as to interfere greatly with the patient's ability to obtain sufficient air through the trachea to supply the respiratory demands. Not only is the tongue pushed upward and backward, but increased tension is made on the mylohyoid muscle. With this increase of tension on this muscle, there is necessarily an upward and forward displacement of the hyoid bone. In several days and sometimes in a few hours this tension is so great as not only to pull the jaw down but to pull the hyoid bone forward and slightly upward. Of course, the fibrous attachments between the hyoid bone and the larynx are such that when the hyoid bone is displaced the larynx is carried with it. With the base of the tongue pushed backward to the retropharynx and the larynx pulled upward and forward, it is easily understood why the patient fights so frantically for breath (fig. 5).

With a patient in this condition any anesthetic is dangerous. Frequently the patient's condition is such as to demand an immediate tracheotomy. This is usually done with the aid of local anesthesia, and then one of the gas anesthetic agents can be administered through the tracheotomy tube. If the patient's condition is not so desperate as to demand an immediate tracheotomy, one of the intravenous anesthetics, preferably sodium pentothal (sodium-1-methylbutyl-thiobarbituric acid) can be employed, but even then the tracheotomy set should be handy, as these patients sometimes have embarrassment of respiration after administration of any intravenous anesthetic.

Whenever an intravenous anesthetic is employed, it should be given by the intermittent fractional method of injection. Dr. R. Charles

Adams has stated that pentothal sodium should not be given to a patient who has been receiving sulfanilamide, but Dr. Perrin Long has expressed disagreement with this view. I know of no case in which there have been any disastrous consequences which could be attributed to such a practice. If the patient's condition is such as to warrant the employment of a general anesthetic, my preference is for ethylene. Preliminary administration of morphia and atropine sulfates aids in the giving of any anesthetic. Oxygen, carbon dioxide and coramine (a 25 per cent solution of pyridine betacarbonate in diethylamine) should be handy. The employment of helium in association with either nitrogen monoxide or ethylene has not yet reached the stage of practical application. However, helium can carry oxygen through greatly restricted

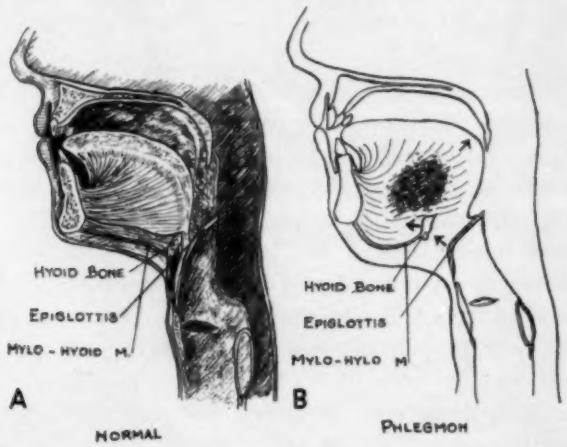

Fig. 5.—Diagrammatic sketches. Note that as the phlegmon increases it pushes up the tongue to the back of the mouth and pulls the hyoid bone and the epiglottis forward.

respiratory passages, and these patients frequently need quickly all the oxygen possible to be obtained.

Certainly if tension is to be relieved in these cases more than simple incision and drainage will have to be done, for as a rule very little pus will be found. Necrotic and gangrenous material should be removed. Rehn has advocated the routine removal of the submaxillary gland, but this gland should not be removed unless it is involved in the inflammatory process or is interfering with drainage. Care should be exercised to prevent the dissection from extending through the mucous membrane into the mouth.

Most authorities consider that in this type of infection, extension takes place through fascial planes and not by lymphatic channels. It is

also probable that extension can and does take place by both fascial planes and lymphatic routes. In any event, it is certain that free and full drainage is indicated.

In order to meet these indications the incision should start near the angle of the jaw and about ½ inch (1.3 cm.) from the border and continue to the chin. If the infection is bilateral, as it frequently is, this incision should continue in the same manner on the opposite side of the jaw. It should continue through the deep cervical fascia to the muscles of the mylohyoid muscle. When the fibers of this muscle are reached they should be cut transversely. The anterior belly of the digastric muscle should also be cut transversely. By cutting these muscles in this manner the pull on the hyoid bone is released, which is not the case with any incision which enters the deep structures by simply separating the fibers of the mylohyoid muscle. I recall 1 case

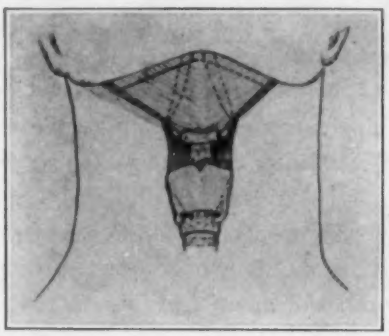

Fig. 6.—Diagram to indicate the necessity for cutting the fibers of the mylohyoid muscle and the digastric muscle transversely if traction on the hyoid bone is to be released.

in which a transverse division of these muscle fibers allowed the larynx to drop back to its normal place, with great relief to the respiratory efforts of the patient (fig. 6).

The respiratory relief in this case occurred almost immediately and before the incision extended to the involved tissues under the tongue.

In a life-saving procedure such as this operation often is, no consideration should be given to the possible appearance of the scar after the patient's recovery, for only the saving of life is the objective of the surgical attack in such cases.

The incision is packed with gauze and left wide open so as to allow free and full drainage.

If considered advisable a simple, safe plastic operation in the future will often greatly improve the appearance of the scar, but this is seldom indicated.

CARDIAL* GASTRIC ULCERS

RESULTS OF OPERATION FOR APPARENTLY INACCESSIBLE LESIONS

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Experience has shown that in the evolution of treatment cycles occur. This may be due to the changing incidence of the disease or to its severity. Of great influence, of course, are the results which follow different methods of treatment. Generally speaking, response to conservative methods of treatment is more likely to occur when economic and social changes have improved the general health of the community. Under such circumstances, routine methods of therapy may produce an increasing incidence of benefit or cure, which increases further when improved methods of therapy are developed and instituted.

These remarks apply particularly well to the treatment of gastric ulcers. As a result of a better understanding of these lesions and their earlier recognition, while the lesion is still small and without the complicating features of hemorrhage, perforation and obstruction, relief of symptoms and healing of the ulcer have resulted from a medical regimen in more cases recently than many years ago. The only objection to a medical regimen in all such cases is that in some of them the lesion, instead of being a small gastric ulcer, is in reality ulcerating carcinoma. In many such cases roentgen or gastroscopic examinations will not assist in the differential diagnosis (table 1). It has been said that a trial course of medical treatment serves as a diagnostic aid, for, if the patient is relieved of symptoms, if the ulcer disappears roentgenographically and if blood disappears from the stools, then the lesion is benign. Clinical experience, however, has demonstrated that in some cases of malignant gastric ulceration these criteria may seem to be satisfied but the lesion does not heal; it only seems to do so, for, as Schindler [1] has shown, the carcinomatous process may extend from the margin of the ulcer into the crater, obliterating it.

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* In this paper the adjective "cardial" is used in reference to the cardia, in contradistinction to "cardiac," which is generally used in reference to the heart.

From the Division of Surgery, the Mayo Clinic.

1. Schindler, R.: Gastroscopy, Chicago, University of Chicago Press, 1937, p. 257.

The incidence of malignant changes in gastric ulcers has been stated to be from 10 to 20 per cent. Walton [2] said that the figures of Stewart [3] are now generally accepted. He concluded that in 9.5 per cent of cases chronic ulcer becomes carcinomatous and that carcinoma originates in a chronic ulcer in 17 per cent. Katsch,[4] however, reported an incidence of 20 per cent. Finsterer [5] found that in 532 cases of resection for gastric ulcer the ulcer was carcinomatous in 141, an incidence of "20.9 per cent." In 41 the lesion was diagnosed clinically as gastric ulcer, and the surgeon concurred in the diagnosis on macroscopic examination at the time of operation; histologic examination by a competent pathologist, however, revealed early carcinoma. In 55 cases gastric ulcer was diagnosed clinically, but at operation the surgeon and the pathologist were able to make a diagnosis of carcinomatous ulcer. Chamberlain,[6] in Moynihan's clinic, in a follow-up study of 216 patients treated for suspected benign gastric ulcer, found that 9.5 per cent of the group had

TABLE 1.—*Roentgen Diagnosis in Seventy-Six Cases of High Gastric Lesions in Which Examination Was Performed in 1938 and 1939*

	Cases	Per Cent
Correct roentgen diagnosis	67	88
Unqualified correct diagnosis	54	71
Ulcerative lesion; unable to say whether benign or malignant	13	17
Incorrect roentgen diagnosis (lesion described as benign when malignant and vice versa)	7	9
Negative roentgen report	2	3

died of carcinoma of the stomach. Balfour [7] said that the subsequent death rate of patients operated on for duodenal ulcer is not greater than that of the general population of similar age and sex but that the subsequent death rate of patients operated on for gastric ulcer is three times as great as that of the general population. Gastric carcinoma is the most important single factor influencing life expectancy.

The possibility of healing a large gastric ulcer with a crater 1.5 cm. or larger in diameter by other than surgical methods should be looked on with skepticism, for all such ulcers have a tendency to perforate.

2. Walton, J.: Carcinoma of the Stomach, Lancet **1**:1101-1107 (May 16) 1936.

3. Stewart, cited by Portis, S. A., and Jaffé, R. H.: A Study of Peptic Ulcer Based on Necropsy Records, J. A. M. A. **110**:6-13 (Jan. 1) 1938.

4. Katsch, cited by Hurst, A. F.: Carcinoma of the Stomach, Lancet **2**: 1455 (Dec. 18) 1937.

5. Finsterer, H.: Malignant Degeneration of Gastric Ulcer, Proc. Roy. Soc. Med. **32**:183-196 (Jan.) 1939.

6. Chamberlain, D.: Partial Gastrectomy for Gastric Ulcer, Surg., Gynec. & Obst. **45**:513-517 (Oct.) 1927.

7. Balfour, D. C.: Factors Influencing the Life Expectancy of Patients Operated on for Gastric Ulcer, Ann. Surg. **76**:405-408 (Sept.) 1922.

Patients with such lesions usually have had clinical evidence of perforation of the ulcer either to the gastrohepatic omentum or to the pancreas, and many of them have had hemorrhages. When such lesions occur, surgical removal of the lesion affords the best chance of permanent cure and does it in a reasonably short time. This statement is true regardless of the age of the patient if his condition is otherwise satisfactory. Furthermore, surgical removal relieves the menace of fatal hemorrhage from the lesion or of an acute perforation which may require an emergency procedure for its closure. Of great importance is the removal of a lesion which may be malignant or may become so.

The risk of the operation for gastric ulcer should not exceed a maximum of 5 per cent, and it is possible to operate on a large series of patients with gastric ulcer with a mortality rate of considerably less than 5 per cent. In point of fact, in 215 resections performed at the Mayo Clinic in 1938 for benign lesions of the stomach and duodenum, the mortality rate was 2.8 per cent.[8] There were 43 partial gastrectomies for gastric ulcer, with a mortality rate of 2.3 per cent. The cases were selected carefully, and partial gastrectomy was performed only when the nature of the lesion and the condition of the patient warranted this procedure. The results of a properly chosen, properly performed operation for gastric ulcer are some of the best in surgical practice, for recurrence of the ulceration is rare. I have not seen recurrence of gastric ulcer or gastrojejunal ulcer after partial gastrectomy for gastric ulcer when half or more of the stomach has been removed. Recurrence of ulcer, in my experience, is rare when the gastric ulcer has been excised and gastroenterostomy performed.

In the experience of this clinic the large gastric ulcers are most frequently present along the lesser curvature of the stomach or slightly posterior to it. In Stewart's extensive series 3.5 per cent of the lesions occurred on the gastric side of the pyloric canal; 22.4 per cent were 1 to 2 inches (2.5 to 5 cm.) from the pylorus; 34.1 per cent were 2 to 3 inches (5 to 7.5 cm.) from the pylorus; 29 per cent were 3 to 4 inches (7.5 to 10 cm.) from the pylorus, and 10.6 per cent were more than 4 inches (10 cm.) from the pylorus. On reviewing 272 cases of chronic gastric ulcer in which operation was performed at the Mayo Clinic from Jan. 1, 1933, to Jan. 1, 1937, Clagett and I[9] found that 66.9 per cent of the ulcers were at or above the incisura angularis, 15

8. Walters, W.; Gray, H. K., and Priestley, J. T.: Surgical Report for 1938 on Lesions of the Stomach and Duodenum, Proc. Staff Meet., May Clin. **14**:807-814 (Dec. 20) 1939.

9. Walters, W., and Clagett, O. T.: The Surgical Treatment of Chronic Gastric Ulcer: Review of Two Hundred and Seventy-Two Cases, Surg., Gynec. & Obst., to be published.

per cent were on the posterior wall and 1.5 per cent were on the greater curvature. The remainder were below the incisura angularis.

In several of the cases at the clinic the ulcer appeared on roentgen examination to be located very high on the lesser curvature, and for this reason it was thought that operative removal would be difficult; it was found at operation, however, that perforation of the lesion to the capsule of the pancreas had given an erroneous idea of the amount of stomach between the ulcer and the esophagus. In these cases there was actually much more uninvolved stomach than the roentgenogram indicated (table 1). On other occasions the early division of the gastrohepatic omentum at a very high level assisted in mobilizing the upper part of the stomach so that unusually high lesions could be removed without too great difficulty. Two observations led me to study a series of patients operated on for benign and malignant lesions situated midway between the incisura angularis and the esophagus or higher. These were as follows: (1) recognition of the fact that the roentgenologic appearance of a gastric ulcer can be so misinterpreted that necessary surgical procedures may be postponed and (2) a general impression that, although removal of a gastric ulcer is made more difficult when it is situated above the incisura angularis, the mortality rate from the operation is not increased appreciably. Finsterer [10] and Rieder [11] called the gastric ulcers situated in this region subcardial or juxtacardial ulcers.

During 1938 and 1939 at the Mayo Clinic there were 42 cases in which operation was performed for benign lesions situated in the cardial region, with 1 death, a mortality of 2.3 per cent (table 2). In 3 the lesions removed were polyps; in 2, diverticula; in 1, a leiomyoma, and in 1, a cyst. Local excisions were performed in 6 of these 7 cases, and partial gastrectomy was performed in 1. There were no deaths. Thirty-five patients who had cardial benign gastric ulcers were operated on. Twenty-six partial gastrectomies were done for cardial gastric ulcers, with 1 death, a mortality of 3.8 per cent. In 4 cases the ulcer was excised, and gastroenterostomy was performed. In 1 case excision of the ulcer was done, and in 4 cases gastroenterostomy was performed. In these 9 cases there were no deaths.

In 34 cases in which cardial carcinoma was present surgical treatment was possible (table 2). In all but 1 gastric resection was performed; that is, partial gastrectomy in 28 and total gastrectomy in 5. In these 34 cases the mortality rate was 14.7 per cent. This mortality rate for operations for malignant disease in the upper part of the

10. Finsterer, H.: Das cardianahe Magengeschwür, Wien. klin. Wchnschr. **52**: 394-400 (April 28) 1939.

11. Rieder, W.: Chirurgische Behandlung des kardianahen Ulcus ventriculi, Arch. f. klin. Chir. **196**:640-655, 1939; abstracted, Internat. S. Digest **29**:21-22 (Jan.) 1940.

stomach is in keeping with that following partial gastrectomy performed for all types of carcinomas of the stomach in the year 1938 at the clinic, which was 13.5 per cent (126 cases [8]).

The relative incidence of gastric lesions in the cardial portion of the stomach during 1938 and 1939 is of interest. There were 76 cardial lesions among the 542 gastric lesions for which operation was performed, an incidence of 14 per cent. In other words, 14 per cent of the patients with gastric lesions who underwent operation during the years 1938 and 1939 at the Mayo Clinic had lesions located in the cardial region. Finsterer,[10] in the course of 532 resections of the stomach for gastric ulcer, found 124 subcardial lesions, or 23.3 per cent.

TABLE 2.—*Operative Procedures and Mortality Rates in Seventy-Six Cases of High Gastric Lesions in Which Operation Was Performed During 1938 and 1939 at the Mayo Clinic*

	Cases	Deaths	Mortality Rate, per Cent
All benign high gastric lesions	42	1	2.3
Benign gastric ulcers	35	1	2.8
Partial gastrectomy	26	1	3.8
Cautery excision or excision and gastroenterostomy	4	0	0
Simple excision	1	0	0
Gastroenterostomy	4	0	0
Miscellaneous benign lesions	7	0	0
Polyposis of stomach	3	0	0
Diverticula	2	0	0
Leiomyoma	1	0	0
Cysts of cardia (all excised except 1 cyst and 1 hemangioma)	1	0	0
High gastric carcinoma	34	5	14.7
Posterior Polya operation with or without modifications	15	2	13.3
Anterior Polya operation with enteroanastomosis	9	0	0
Total gastrectomy	5	2	40
Segmental resection of the stomach	2	0	0
Transgastric excision of lesion	2	1	50
Palliative posterior gastroenterostomy	1	0	0

Finsterer [10] and Rieder [11] both reported with favor on high gastric resection with removal of the ulcer whenever possible, and both advised the Kelling-Madlener type of subtotal gastrectomy, which allows the ulcer to remain in situ when it is situated too high to remove with safety. It is felt that by removal of the greatest acid-forming portion of the stomach more permanent cure is effected. In this procedure, which was originally proposed by Kelling [12] in 1918 and was described and brought into favor by Madlener [13] in 1923 and 1929, resection of the stomach below the ulcer is accomplished by anastomosis of the stomach to the duodenum by the Billroth I type of procedure. Fin-

12. Kelling, G., cited by Finsterer.[10]

13. Madlener, M.: Ueber Pylorektomie bei pylorusfernem Magengeschwür, Zentralbl. f. Chir. **50**:1313-1317, 1923; Ergebnisse der "palliativen" Resektion beim pylorusfernem Magengeschwür, ibid. **56**:2694-2696, 1929.

sterer [10] has reported anastomosis posterior to the colon of the end of the stomach to the side of the jejunum in the palliative resection when fixation of the duodenum might cause tension on the suture line. Lewisohn [14] stated that he does not favor the Madlener procedure, for the postoperative results of Madlener's operation when viewed in large numbers are unsatisfactory; the ulcer is not put at rest and gastric acidity is seldom sufficiently high preoperatively to require gastric resection for its reduction.

My impression coincides in some ways with these opinions. I believe that every gastric ulcer should, if possible, be removed by partial or subtotal gastric resection or, in less satisfactory conditions, by excision with or without gastroenterostomy. However, if the patient's condition is too poor to withstand resection or excision, gastroenterostomy is favored, for after gastroenterostomy for gastric ulcer a relatively high incidence of achlorhydria occurs, and healing of the ulcer frequently is obtained.[15] The mortality from such a procedure for chronic gastric ulcer in 228 operations, Eusterman and Balfour [16] stated, was 1.7 per cent, whereas in 540 cases of gastroenterostomy for acute, subacute and chronic gastric ulcer it was 3.9 per cent. Many of the patients for whom the operation was selected were poor surgical risks, or their condition was considered unfavorable for gastric resection; yet the results were good, for Eusterman and Balfour [16] found that 79 per cent of 100 patients with gastric ulcer for which gastroenterostomy was performed were well five years after operation, and 4 per cent were fairly well. Eusterman and Balfour stated that the operation protects against reactivation of the ulcer in more than 90 per cent of the cases and also protects against perforation and obstruction.

Clagett and I, in a study of 272 consecutive operations for gastric ulcer performed at the Mayo Clinic from Jan. 1, 1933, to Jan. 1, 1937, reported that 16 patients had undergone posterior gastroenterostomy, and 5 anterior gastroenterostomy with enteroenterostomy. Fourteen of these patients reported that they were in excellent health without distress of consequence after this type of operation, and 1 reported occasional mild distress. There was no report from 5 of the group. The average gain in weight was 15 pounds (6.8 Kg.). One hundred and sixty-two of the 272 patients underwent partial gastrectomy.

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14. Lewisohn, R.: Problems in the Surgical Treatment of Chronic Duodenal Ulcers, Ann. Surg. **111**:355-361 (March) 1940.

15. Walters, W.: Gastric Acidity Following Operations for Gastric and Duodenal Ulcer: Its Effect on the Question of Partial Gastrectomy, Ann. Surg. **104**:585-593 (Oct.) 1936.

16. Eusterman, G. B., and Balfour, D. C.: The Stomach and Duodenum, Philadelphia, W. B. Saunders Company, 1935, pp. 469-471 and 505-514.

Gastrojejunal ulcer is very infrequent after gastroenterostomy for gastric ulcer. Thus, it seems that the good results and the excellent chance for relative achlorhydria from a simple operation with a low operative mortality may be preferable to a higher risk associated with resection when the ulcer cannot be removed. Jejunostomy is not favored because of the necessity of prolonged difficult treatment and the frequency of recurrence after closure of the opening.

As experience develops it will be found that more high gastric lesions will be found resectable. In this series of 35 cardial ulcers, partial gastrectomy was performed in 31 instances, or 88 per cent.

Fig. 1.—Gastric ulcer 2 cm. below the esophagus for which partial gastrectomy of the Hofmeister-Polya type was performed, with removal of the ulcer.

The illustrations and the abbreviated report of cases were selected not to demonstrate any special point but merely because they illustrate characteristic lesions of the type under consideration.

REPORT OF CASES

CASE 1.—A man 60 years of age was admitted to the clinic Nov. 1, 1939, complaining of anorexia, loss of 40 pounds (18.1 Kg.) and constipation of nine months' duration. Roentgen examination of the stomach revealed a gastric ulcer 2 cm. in diameter high on the lesser curvature (fig. 1). On gastric analysis before operation the total acidity was 50 and the free acids 40 (Töpfer's method). At operation an inflammatory gastric ulcer 2 cm. below the esophagus was found which had perforated into the gastrohepatic omentum. Partial gastrectomy of the posterior Hofmeister-Polya type was performed, with removal of three fourths of the stomach, including the gastric ulcer. The postoperative convalescence was uneventful. After operation the total acidity was 6, and there was no free acid.

Fig. 2.—Gastric ulcer 3 cm. below the cardia for which partial gastrectomy of the posterior Polya type was performed, with removal of four fifths of the stomach, including the ulcer.

Fig. 3.—Extensive carcinoma of the stomach extending almost to the esophagus, for which partial gastrectomy of the posterior Polya type was performed, with removal of the lesion.

CASE 2.—A woman 64 years of age registered at the clinic on Aug. 7, 1939, complaining of intermittent epigastric distress of ten years' duration and of chills, fever, nausea, vomiting and severe pain in the epigastrium and back of three weeks' duration. Roentgen examination of the stomach revealed an ulcer high on the lesser curvature of the stomach (fig. 2). At operation an inflammatory gastric ulcer was found 3 cm. below the esophagus, with a crater 1.5 cm. in diameter. Partial gastrectomy of the posterior Polya type with removal of four fifths of the stomach, including the gastric ulcer, was done. The patient was well four months later.

CASE 3.—A man 58 years of age entered the clinic Nov. 21, 1939. He had had epigastric distress for twenty years and had lost 30 pounds (13.6 Kg.) in the previous year. Roentgen examination of the stomach revealed extensive ulcerating carcinoma involving almost the entire stomach, which was probably inoperable (fig. 3). Gastric analysis (Töpfer's method) revealed a total acidity of 14 and

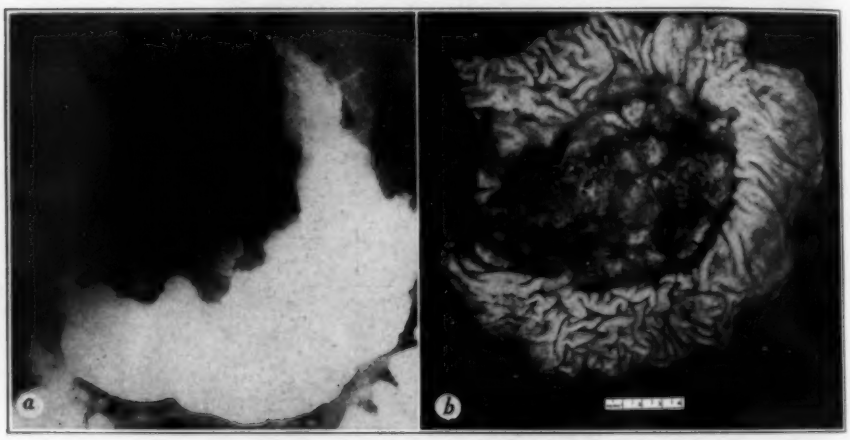

Fig. 4.—Huge ulcerating carcinoma involving all of the lesser curvature of the stomach; *a*, roentgenogram; *b*, carcinomatous ulcer removed at operation; partial gastrectomy of the posterior Hofmeister-Polya type was performed.

no free acid. Partial gastrectomy of the posterior Polya type was performed, with removal of four fifths of the stomach for ulcerating perforating adenocarcinoma grade 2 (on a grading basis of 1 to 4). The growth measured 9 by 9 by 3 cm. and extended almost to the esophagus. The convalescence was uneventful.

CASE 4.—A man aged 63 years came to the clinic July 13, 1939, complaining of gastric distress, weakness and loss of 24 pounds (10.9 Kg.) in the previous three months. Roentgen examination of the stomach revealed ulcerating carcinoma of the middle third and upper portion of the body of the stomach. The roentgenologist felt that operability was doubtful (fig. 4a). Partial gastrectomy of the posterior Hofmeister-Polya type was done to remove four fifths of the stomach for a lesion which extended almost to the esophagus. The pathologist reported adenocarcinoma, grade 2, measuring 15 by 10 by 3 cm. (fig. 4*b*); this

was the largest carcinomatous ulcer ever removed at the clinic. The patient died after operation from bronchopneumonia.

CASE 5.—A woman aged 42 years entered the clinic Nov. 27, 1939, on account of weakness and three gastric hemorrhages in 1938 and 1939. Roentgen exami-

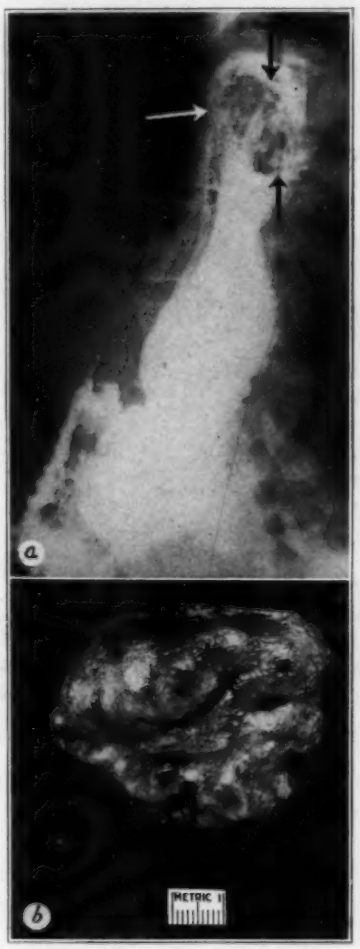

Fig. 5.—Leiomyoma of the cardiac end of the stomach; *a*, roentgenogram; *b*, specimen removed by transgastric excision.

nation of the stomach showed a large polypoid tumor near the cardia (fig. 5*a*). Gastric analysis revealed a value for total acidity of 84 and for free acid of 70. Excision through a transgastric approach revealed a leiomyoma, measuring 6 by 5 by 3 cm. (fig. 5*b*), which arose from the posterior wall of the cardial area of the stomach. The convalescence was uneventful.

CASE 6.—A woman, aged 52 years, was admitted to the clinic Sept. 26, 1939, because of symptoms of peptic ulcer of six weeks' duration and hematemesis and melena of two weeks. Roentgen examination of the stomach revealed polyposis of the middle third and two polyps high in the stomach (fig. 6). On gastric analysis total acidity was 10, and there was no free acid. Transgastric excision of multiple adenomatous polyps was done. The patient's convalescence was uneventful.

SUMMARY

Seventy-six, or 14 per cent, of the 542 gastric lesions for which operation was performed at the Mayo Clinic during 1938 and 1939 were found to be at or higher than a point midway between the angle of the stomach and the esophagus. In 35 of the 76 cases benign gastric ulcer was present. In 26 of the 35 cases of benign gastric ulcer situated high above the incisura angularis of the stomach partial gastric resection was performed, with 1 death. There were 34 cases of carcinoma in which the lesion was situated high above the incisura angularis of the stomach; some form of gastric resection (partial or total gastrectomy) was done in all but 1, with 5 deaths. In 7 cases miscellaneous benign lesions were removed by local excision, without mortality.

Frequently the high gastric lesion appeared higher in the roentgenogram than it actually was, because of foreshortening of the stomach proximal to it, caused by perforation of the ulcer onto the pancreas or into the gastrohepatic omentum. In most such cases ample stomach

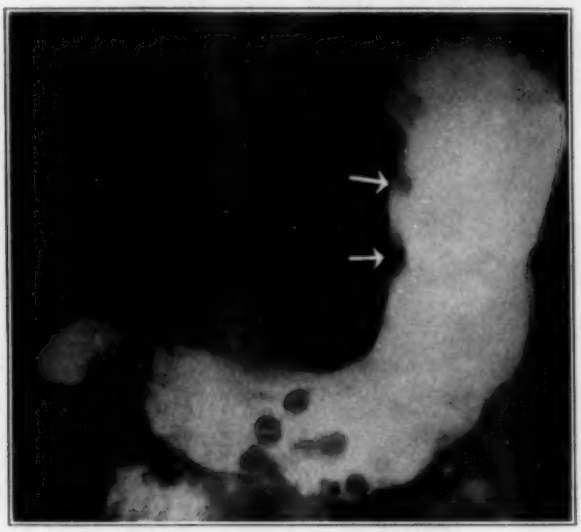

Fig. 6.—Polyposis of the stomach. There were two polyps in the vicinity of the cardia. Transgastric excision was performed.

could be found above the lesion for safe partial gastric resection after mobilization of the stomach and its perforating process and by high ligation of the gastrohepatic omentum.

Partial or subtotal gastrectomy was preferred for the surgical treatment of cardial gastric ulcer. When the condition of the patient did not allow this, excision of the lesion with or without gastroenterostomy was favored. When the ulcer could not be excised with safety because of its proximity to the esophagus or because of the poor condition of the patient, gastroenterostomy was preferred, as a high incidence of relative achlorhydria and healing occurred after such a procedure. The Kelling-Madlener palliative gastric resection, in which the ulcer is not removed, has not been utilized by us.

The difficulty of differentiating a malignant from a benign ulcerative process in the cardial gastric region by roentgen examination was emphasized.

The material in this paper relative to cardial ulcers and to the follow-up study of cases has been assembled with the aid of Dr. William H. Cleveland, assistant surgeon, the Mayo Clinic.

SUBDELTOID BURSITIS

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Some six years ago, when Dr. Dean Lewis was visiting me in San Francisco, I happened to bring up the subject of his system of surgery and how much he had included in it which was obsolete. When he asked me to be more specific, I called his attention to the fact I had discovered that the proper treatment of subdeltoid bursitis seemed to be unknown generally and that the old advice about diathermy, etc., was still given in his published work. I called his attention to the immediate relief of 90 per cent of this pain in the shoulder obtained by simple needling, which eases the tension in a dense, mesothelium-lined fibrous sac. He frankly stated that he had never heard of this treatment and told me that some day he would publish a one volume treatise on general surgery which would leave out everything obsolete and would include everything useful that one book would hold. I am still hoping for this volume.

Dr. Lewis urged me to publish my method of treatment in the *International Clinics,* which I did in 1936,[1] and now, for his birthday issue of the ARCHIVES, I think it fair that this subject should be brought up again, because it is quite evident that this proper treatment for inflammation, whether traumatic or otherwise, of the subdeltoid bursa is not yet universally approved. This was particularly brought to my attention by the work of Ferguson,[2] as short a time ago as May 1938. On reading his résumé, I again took up the subject with a number of my professional friends, especially orthopedic and general surgeons, and discovered that there is still some question about it.

The subdeltoid bursa may in some instances be connected with the shoulder joint, but because in all my cases of acute subdeltoid bursitis the symptoms are referable only to the bursa I have reason to believe that none of the bursae observed by me has been so connected. A great number of physicians now agree that 90 per cent of pains of any moment about the shoulder are due to an irritation within the subdeltoid bursa, and certainly the pain of an acute inflammation of this sac is so much more agonizing and incapacitating than any other that a simple pro-

1. Weeks, A.: Subdeltoid Bursitis (Acute), Internat. Clin. **3**:40-48 (Sept.) 1936.

2. Ferguson, L. K.: Shoulder Pain and Disability Due to Lesions of Subdeltoid Bursa and Supraspinatus Tendon: Five-Year Collective Review, Internat. Abstr. Surg. **66**:472-487, 1938; in Surg., Gynec. & Obst., May 1938.

cedure for its quick relief should be known universally. From the literature it is apparent that there have been so many misunderstandings about why the pain is relieved that I hope I am specific enough when I say that it is not the procaine hydrochloride or any other factor in the way of washing out the bursa between two needles or putting in a sclerosing solution that relieves the pain. It is simply relief of tension afforded by puncturing the firm-walled sac in numerous places with a needle. This amounts, of course, to the same thing as making an operation of it and laying open the sac with a knife, but it is so much simpler and can be done so easily in the office that there is little excuse for any delay or any added expense. Since my last report I have had some 40 patients in whom immediate relief was produced by needling only, and but 1 of these had any history of trauma. In other words, most patients with this condition have a history of infections connected with the nose, throat or teeth.

I first used this treatment for acute subdeltoid bursitis in 1908, purely as a diagnostic procedure, common then, because I suspected the presence of fluid in the region. The relief of pain was so instantaneous on aspiration of about 1 cc. of straw-colored fluid that I have applied it ever since, supposing it to be well known.

In 1913, Prof. J. M. Flint, of New Haven, Conn., suggested aspiration for acute traumatic bursitis but said nothing about this treatment for all forms of the disease. If he had done so, no doubt it would have been popularized long since, and much suffering might have been prevented.

Some of my friends who are orthopedic surgeons report that unless the calcium in the bursa has organized to the consistency of bone they are now treating the chronic forms of subdeltoid bursitis by thorough needling. This seems to change the blood supply and causes more rapid absorption of the salt. In other words, these surgeons find an operation unnecessary unless the deposit of salt has become bonelike. One of my friends told me last year that he had had, in the past three or four years, some 15 patients suffering from subdeltoid bursitis and that he never bothered any more to do the operation with the region under local anesthesia, because, of course, it is impossible to inject enough procaine hydrochloride into this painful sac to prevent some agony with the needling. He therefore now gives the patient a whiff of nitrogen monoxide and, as he expresses it, needles the bursa fanwise in all directions, from the outside well over into the region of the supraspinatus tendon. In no case has he failed to give immediate relief when the disease was acute. Of course, when a patient has suffered for two weeks with this agonizing disease, has been kept awake and has been unable to tolerate any motion whatever in the shoulder joint, there is bound to be some disability from the lack of use and from the outrage

to the associated nerves, but these disabilities are quickly forgotten when the acute agony has been relieved. All of the patients who have been under treatment and have suffered all of the old abuses, especially diathermy, say after treatment with diathermy their pain is increased a great deal. This, of course, is due to the heat, which causes more congestion and more tension in the tight sac.

In conclusion, I venture to say that every patient suffering from subdeltoid bursitis of the acute type, whether the sac contains calcium or not, will be relieved at once if the tension is removed by numerous punctures with a fair-sized needle, whether local anesthesia with procaine hydrochloride only or general anesthesia is used. Chronic conditions also will be relieved and the calcium absorbed after use of the same method, unless the salt has organized into bony hardness, in which case surgical removal is justified.

OPERATIVE TREATMENT OF TRUE HERMAPHRODITISM

A NEW TECHNIC FOR CURING HYPOSPADIAS

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BALTIMORE

Hermaphroditism has interested the members of the medical profession since earliest days, but until recent years the clinical descriptions and the anatomic and microscopic studies were so inadequate that many early reports are not acceptable today.

In 1924 I reported a case of true hermaphroditism which at that time was the ninth case acceptable by scientific standards. In 1937 I found that 11 additional accepted cases had appeared in the literature. Since then a case, previously questioned, has been shown to be a proved case of hermaphroditismus verus.[1] I wish to present my second case.[2]

REPORT OF A CASE

An East Indian aged 20 came from Johannesburg, South Africa, on Dec. 14, 1937, after having stopped to consult urologists in Italy, France and England. He was referred to me by Dr. Vincent Vermooten. He had been brought up as a male and had no idea that he was anything else. He had normal male sexual desires but had never been able to have intercourse on account of a penile deformity. He had frequently masturbated.

Examination revealed a well developed, slight young man of masculine build, with a sparse growth of hair on the lips and face. There was an abundance of hair on the body and extremities. The breasts were typically male. There were a completely bifid scrotum and a penis of fair size, drawn backward in the scrotal cleft by a pronounced chordee. The urinary meatus was present between the halves of the bifid scrotum (fig. 1). There was a furrow on the ventral surface of the penis, covered with mucous membrane. The right side of the scrotum contained a well developed, apparently normal testis and epididymis. On the

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1. J. F. Gudernatsch (Am. J. Anat. **11**:267, 1911) should be credited with a case of hermaphroditismus verus. The case was excluded by B. Kwartin and J. A. Hyams (J. Urol. **18**:363, 1927), but a careful study of Dr. Gudernatsch's documents shows conclusively, I believe, that his case is entirely acceptable. The total number of acceptable cases, up to the date of publication of my "Genital Abnormalities, Hermaphroditism and Related Adrenal Diseases" (Baltimore, Williams & Wilkins Company, 1937) is therefore 21, instead of 20.

2. This case was reported to the American Urological Association at its annual meeting in Quebec, Canada, on June 29, 1938.

left side there was a large reducible scrotal inguinal hernia (fig. 1). No testicle could be felt. On rectal examination the outlines of the prostate were indefinite. Beneath the rectum was an unusual oblong soft structure. Vigorous massage did not produce any prostatic fluid.

Fig. 1.—Condition before operation. The penis is concealed between the halves of the scrotum.

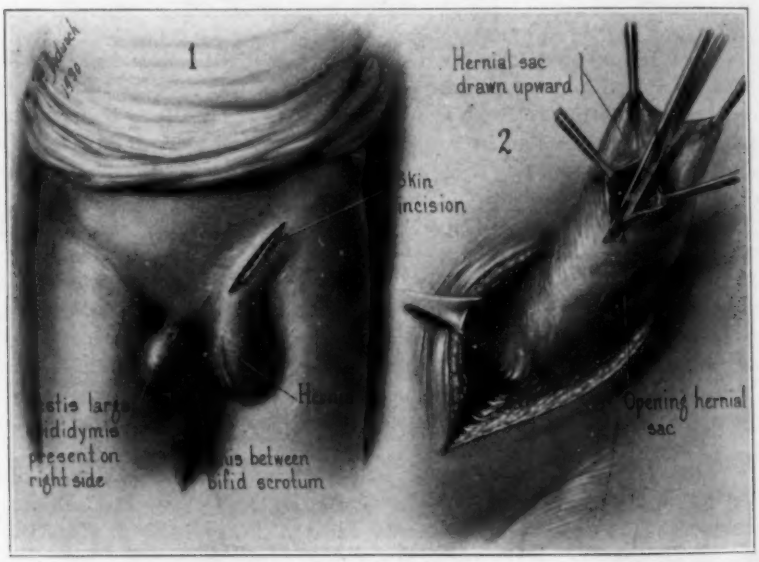

Fig. 2.—Operation for the hernia on the left side. *1*, cutaneous incision; *2*, the sac delivered and opened.

A cystoscope passed easily into the bladder, which was normal. As the instrument was drawn out, Dr. Lloyd G. Lewis was able to make out an opening into which the cystoscope could be introduced. It was evident that the cystoscope

was in a vagina, at the upper end of which the cervix uteri and the os were visible. A solution of 12 per cent sodium iodide was introduced into the cavity, and a uterogram was obtained. Study of the film showed that the fluid extended out into what appeared to be a fallopian tube on the left side.

Roentgenograms of the spine and pelvis showed the bones to have male characteristics.

A determination of urinary estrogen showed no increase (only 4 rat units per twenty-four hour specimen).

A tentative diagnosis of hermaphroditism was made. The case was apparently similar to that reported by me in 1924.[3]

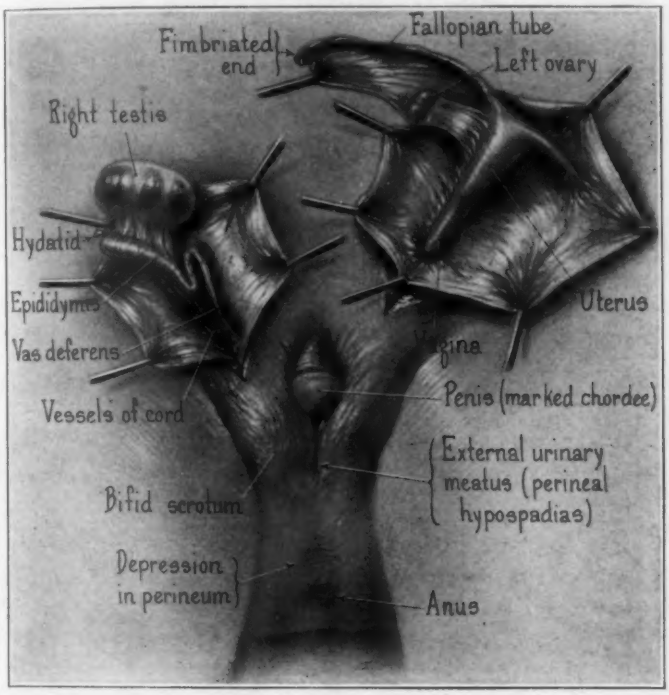

Fig. 3.—After opening the hernial sac on the left side, the uterus, tube and ovary were discovered. At a second operation, several weeks later, the scrotum was opened on the left side, and the testicle and the abnormal epididymis were discovered.

On December 18 a left inguinal hernia was exposed through an oblique incision in the groin (fig. 2). After freeing and opening of the sac a small uterus, a fimbriated left tube and a gonad were seen. The gonad measured 1.5 by 1.6 cm. The tube measured 10 cm. in length. The uterus was 2 cm. in diameter and 4 cm. long and was attached by a stalk, undoubtedly a vagina, that disappeared in the

3. Young, H. H.: Bull. Johns Hopkins Hosp. **35**:165, 1924. Young, H. H., and Davis, D. M.: Practice of Urology, Philadelphia, W. B. Saunders Company, 1926, vol. 2, p. 119.

pelvis beneath the peritoneum. Springing from the other cornu of the uterus was a small cord that was attached to the peritoneum (fig. 3). The gonad was peculiar in appearance. There was no evidence of ovulation, and the structure was different from the normal ovary. Attached to the right cornu of the uterus was a fibrous band that was adherent to the hernial sac. The broad ligament, with a normal blood supply, was present. The question arose whether the gonad was an ovary or a testicle. It was impossible to say definitely what the structure was, but it was small and apparently functionless, and as the patient was distinctly masculine in figure, habits and desires it was decided to remove the uterus, the tube and the gonad (fig. 4). The hernial sac was dissected downward, so that the vagina was isolated

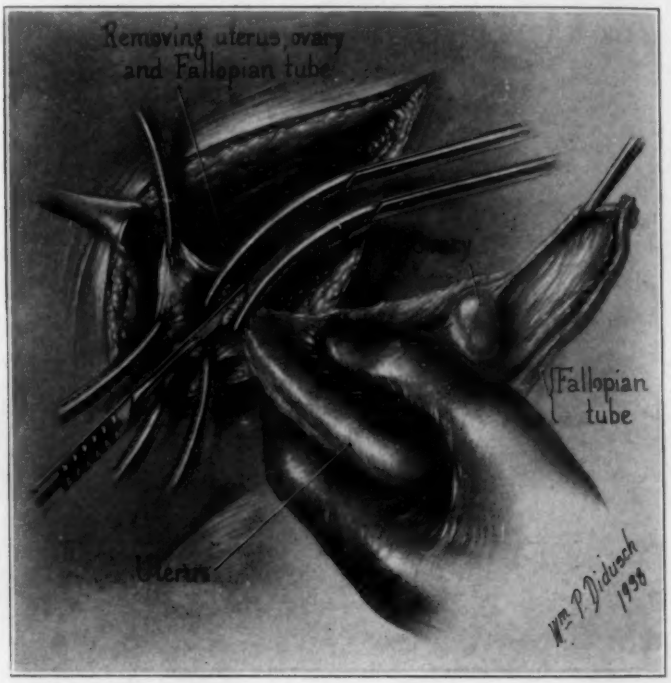

Fig. 4.—Removal of uterus, tube and ovary after division of the vagina through an incision in the left groin.

outside the peritoneum. It was clamped, divided and ligated. The uterus, tube and gonad were removed in one piece with the hernial sac. The edges of the peritoneum were picked up and approximated with chromic catgut suture of the purse-string type. Dr. Lewis then freed the fascia of the external oblique muscle and completed the operation for hernia repair according to the principles of Halsted.

A plastic operation to straighten the penis was carried out by me. The incision extended backward so as to excise the very pronounced congenital chordee. To liberate the penis completely it was necessary to carry out this excision of fibrous tissue down to and between the corpora cavernosa and to free the lower end of the urethra from its attachments and transplant it backward in the perineum. By this technic, which I have carried out in other cases, a large wound was

produced that completely liberated the penis after the skin had been divided on each side (fig. 5). The edges of the skin were then approximated with silver wire sutures that passed through the skin and the septum of the corpora. When tied, this suture drew the two edges of the skin together against the corpora, thus producing a furrow that prevented the formation of a fibrous cord. The penis was held forward against the abdomen by means of a suture through the glans in which a rubber band was interposed to make traction. The wound was covered with silver foil, and a sterilized sea sponge was placed over the paper covering the foil to make gentle pressure. A catheter was not inserted; the patient was allowed to void naturally.

The patient could not void after the operation, and a catheter was introduced and left in place. The wounds healed by first intention. When he was discharged on the twentieth day the chordee had been completely corrected, and the penis

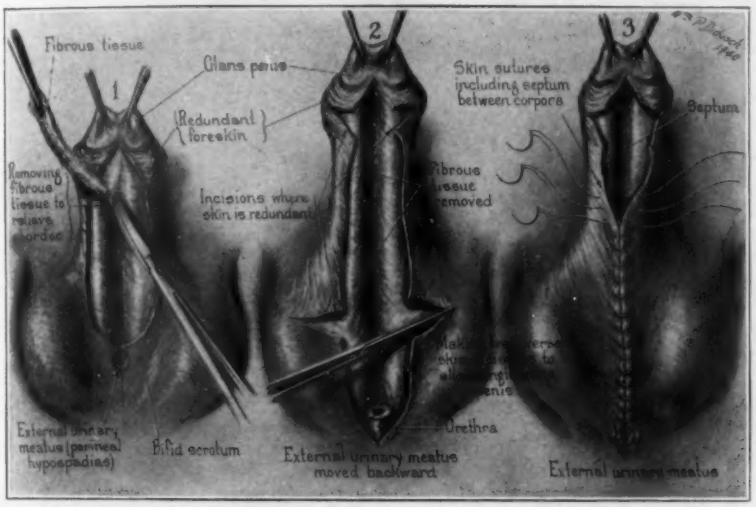

Fig. 5.—Young's operation for hypospadias (first stage). Note the complete removal of the fibrous cord in *1;* transverse incisions through the skin where it is redundant in the foreskin and scrotum, *2;* posterior displacement of the urinary meatus and triple suture to approximate the skin and draw it to the septum between the corpora cavernosa, *3.*

was straight. He was voiding through the urogenital sinus, which opened far back in the perineum. The result of the hernia operation was apparently excellent.

On March 2, 1938, a second operation was carried out with the patient under nitrogen monoxide and ether anesthesia. It consisted of aspiration of material from the testicle and epididymis by Dr. Lewis for spermatozoa. The result being unsatisfactory, an incision was made in the right side of the scrotum, and the testicle was exposed after the tunica vaginalis had been opened. The testicle was larger than normal, measuring 5.3 by 3 by 2.8 cm. The surface was irregular and mottled, similar to the testicle in my other case of hermaphroditismus verus. The epididymis was very abnormal (fig. 3). It did not lie in the usual position next to the testicle. The globus major was attached to the testicle by a thin mass of tissue about 7 mm. long. The body of the epididymis was much smaller and

longer than normal. The globus minor was long and thin. The vas appeared normal. An incision was made in the tunica vaginalis, and through it testicular tissue extruded. This was increased by making pressure on the gland, and by means of scissors a sufficient amount of tissue was removed for biopsy. (This

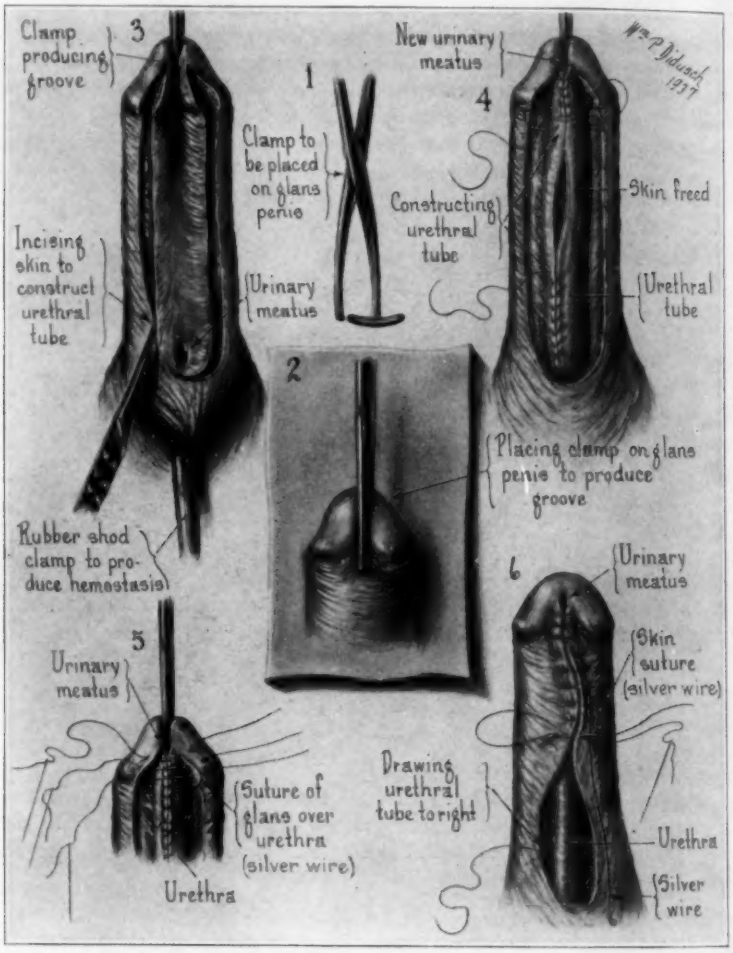

Fig. 6.—Young's modification of the Thiersch plastic operation to form a urethra. *1*, clamp used on the glans; *2*, clamp in place; *3*, cutaneous incisions; *4*, formation of the urethra; *5*, suture of the glans over the urethra; *6*, completion of closure of the skin with vertical mattress sutures.

method is preferable to excising a piece of testis). The wound was then closed by sutures of fine catgut.

The next procedure was to provide drainage through the perineum back of the urinary meatus in the mid perineum. I decided not to attack the vagina. A new urethra was then formed by the method illustrated. The incision on the right side was about 8 mm. from the midline, and on the left, 1.5 cm. (fig. 5).

The incision was carried downward to include the glans. The cut edges of the skin were approximated and inverted by a continuous fine catgut suture with a Duloc needle (fig. 6, *4*). The skin was then approximated with my vertical mattress suture of very fine silver tied over a thread of silver wire (fig. 6, *5* and *6*). (I often use a very delicate rubber tube instead of the piece of silver wire.) Examination showed a good deal of tension of the skin along the last 2.5 cm. of the penis. I therefore made an incision along the dorsum for this distance and at the upper end carried an oblique incision on each side (fig. 7). With the skin freed on each side, no difficulty was experienced in drawing the upper half of the Y down into the lower part of the wound and suturing it there so as to form a V. This procedure, which I have carried out in a number of cases, is

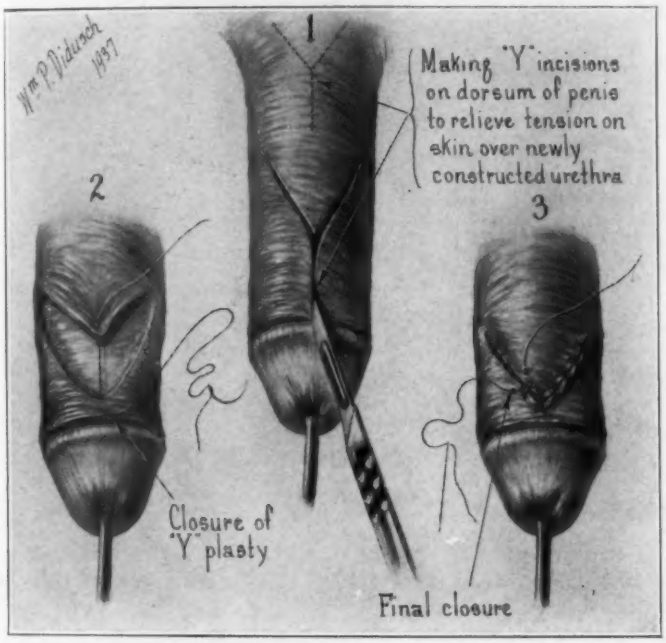
Wm P Didusch 1937
1
Making "Y" incisions on dorsum of penis to relieve tension on skin over newly constructed urethra
2
3
Closure of "Y" plasty
Final closure

Fig. 7.—Y-V plastic operation for the dorsum of the penis, to relieve tension.

very effective in combating tension of the penile skin resulting from the urethral plastic procedure. It also has the effect of drawing the dorsum upward and helping to correct any tendency to chordee. (In some cases I find it necessary to use the Y-V plastic procedure twice along the dorsum [fig. 7, *1*].)

The patient remained in the hospital four weeks. The healing was per primam intentionem, except at one point just back of the glans, where a small fistula formed, and another place nearby. The penis was straight and of normal length. Most of the urine still passed through the perineal urethrotomy wound, through which the catheter emerged.

On June 1 the perineal mucocutaneous fistula was excised; a small catheter was inserted, and the tissue was drawn tight around it, with the hope that when it was removed the urethrotomy fistula would close. The fistulas, one the size of a pinpoint, near the meatus, and the other, about 2 mm. in diameter, 5 mm.

behind the meatus, were present. These were dissected out; the internal orifice was closed with a purse-string suture of fine catgut and the edges of the skin were approximated with vertical mattress sutures of silver tied around the silver wire on each side. The meatus was enlarged by an incision along its roof that divided a valvelike projection. This operation was not entirely successful.

The patient returned a little later, and the previous operation was repeated to close the fistulas that had recurred. The operation was successful in closing the larger fistula, but a minute opening remained immediately behind the meatus in the glans, through which only a most delicate intestinal needle could be passed, and urine continued to come through the original urethrotomy wound. The urethra was dilated. A catheter was passed from the meatus into the bladder, and the perineal mucocutaneous fistula was excised and closed, but it broke down.

Fig. 8.—Final result after the operations to cure the chordee and construct a urethra from the perineum to the meatus. The patient voids normally through the new glandular urethra.

On August 10 the patient reentered the hospital. A suprapubic incision was made to drain the bladder. The perineal fistula was then excised and closed in layers. The very minute fistula in the glans was again closed as before.

The pinpoint opening recurred, and, as all attempts to close it had failed, the small bridge of tissue (only 3 mm. wide) between the meatus and the fistula was incised with scissors, thus enlarging the meatus backward but causing no defect and completely removing the fistula.

The patient was finally discharged on October 4. The operative result was very satisfactory (fig. 8). The penis was straight. The urinary meatus extended only a little farther back than normal. No fistulas were present. Urine was voided freely and in a good stream. The right testis was in the normal position. The left inguinal hernia apparently had been cured. The patient reported that he had had sexual intercourse frequently. Libido was normal, erections were straight and ejaculation was normal and entirely satisfactory. On rectal examination a soft tubelike structure 4 cm. long could be felt immediately beneath the

rectal wall (remaining portion of the vagina). Beneath this a body, apparently the prostate, about two-thirds the normal size, was palpable. The outlines of the seminal vesicles were indefinite. The fluid obtained by prostatic massage showed many leukocytes and some lecithin cells.

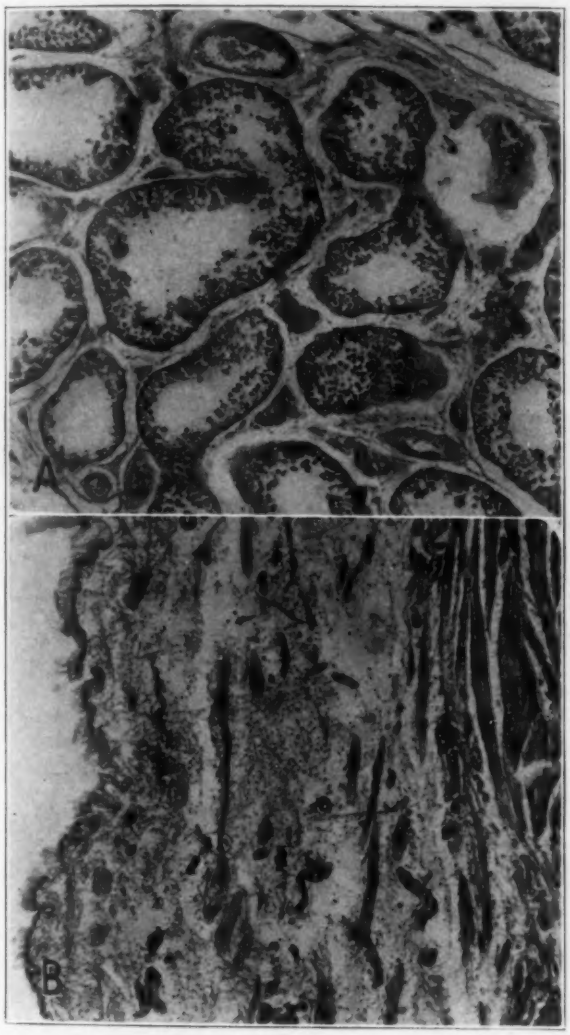

Fig. 9.—Photomicrographs of (*A*) testicle and (*B*) uterus.

Pathologic Report.—Section of the fallopian tube showed a small central canal. Cross section of the ovary showed yellowish white translucent tissue. No follicles were seen. Section of the uterus showed a small cavity that extended downward into the attached portion of the vagina that had been excised.

Microscopic study of the sections of the uterus, the vagina and the fallopian tube (figs. 9 and 10) showed structures typical of these organs. The stroma of the gonad (ovary) was made up of a large number of spindle-shaped cells and fibers arranged in whorls, perfectly typical of ovarian stroma (fig. 10*A*). No

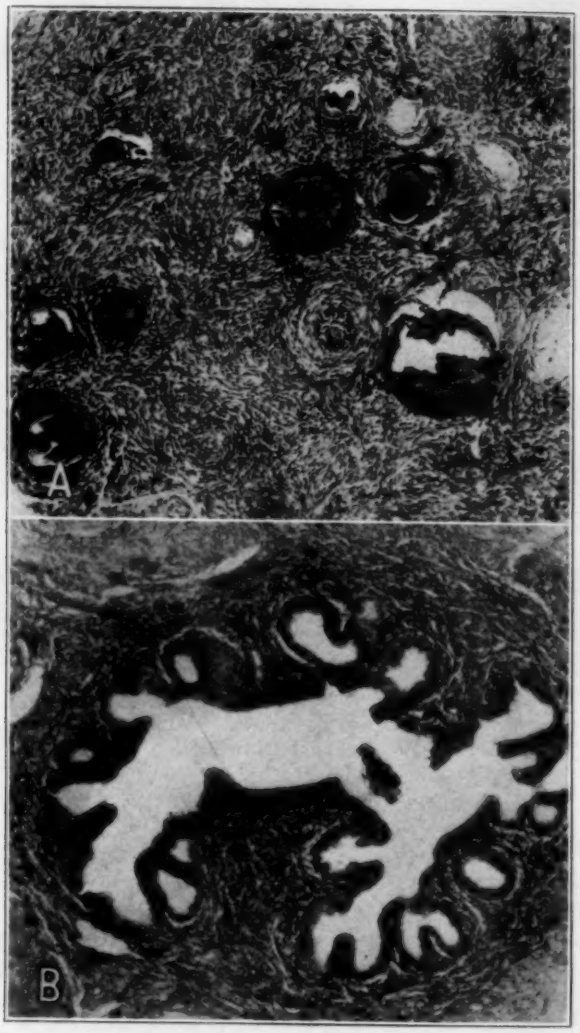

Fig. 10.—Photomicrographs of (*A*) ovary and (*B*) fallopian tube.

definite follicles were seen. In some places there were circular masses of cells suggesting granuloid cells. Surrounding these the stroma cells were concentrically arranged, suggesting the theca interna. Many areas of cylindric calcified so-called psammoma bodies were observed, but no mature follicles and no bodies representing corpora lutea were seen.

Histologic examination of the tissue removed from the right testicle (fig. 9*A*) showed many seminiferous tubules that were normal in appearance. Every stage of spermatogenesis was seen. Sertoli cells were recognized among the larger primary spermatocytes. The interstitial tissue was rather scant, but the cells seemed normal.

The patient has reported to me by letter many times since he left here. On board ship he frequently had intercourse and unfortunately contracted gonorrhea, which was treated in London, England, with success. After he returned to South Africa a small right inguinal hernia that had developed was cured by operation by Dr. Vincent Vermooten. On March 1, 1940, the patient reported by letter that he was normal in every respect.

COMMENT ON THE OPERATIVE TREATMENT

In this case the chordee and the hypospadias were virtually cured by two operations, after which there remained only minute fistulas, two of which were easily cured. The third, in the membranous skin of the glandular urethra, did not close and was simply done away with by enlarging the meatus. The procedures that I employ are much more simple than those usually advocated. The first operation, to cure the chordee, is much more extensive than has been previously employed. Instead of using the various Heineke-Mikulicz procedures, I go in boldly in the median line and excise the cicatricial tissue that produces the chordee, going down to and between the corpora cavernosa until the penis is completely freed of all restricting bands. In order to add to the effectiveness, the urinary meatus is transplanted much farther back in the perineum, thus adding to the freedom of the corpora cavernosa. The use of the triple stitch of fine silver wire that draws the skin in between the corpora prepares the way for the next operation. Abundant skin is afforded by the plan followed, i. e., to divide the skin on each side of the incision at points where it is redundant, viz., near the lower end in the prepuce and in the scrotum. At the second operation abundant skin for the modified Thiersch plastic operation is present, but to insure absolute lack of tension the Y-V plastic operation that I employ on the dorsum is completely effective. A simple, continuous, very fine plain catgut suture with the Duloc needle is then employed to turn in the skin to form a urethra. The newly made urethra is completely covered by drawing together the lateral edges with my vertical mattress suture of extremely fine silver wire that can be tied in a knot over either silver wire or a delicate rubber tube. This suture approximates broad surfaces, and the silver wire, being antiseptic, is an ideal suture material. Two or three minute fistulas usually remain to be closed after this operation. The technic employed is the same; fine plain catgut is used to turn in the urethra and a vertical silver wire mattress suture tied around a rubber tube to close the defect. Since I have adopted these methods I have almost always succeeded in com-

pletely curing the chordee and furnishing a urethra out to the glans penis, so that the patient has had normal urination and also normal sexual powers. I have entirely discarded the many complicated plastic operations described in the literature.

The case of hermaphroditismus verus that I have described belongs to group E in the classification that I made in my book, "Genital Abnormalities, Hermaphroditism and Related Adrenal Diseases." The case is identical with my first one except that the ovary had not gone so far toward complete development and the ovulation was not complete. The patient, however, was just as masculine as in my first case, and his sexual powers were normally male. The operations to cure the hernia, remove the female organs, eradicate the chordee and form a new urethra to the glans penis were entirely successful in both cases.